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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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	:	Examiner: William H. Matthews
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Appln. No. 10/849,990	)	
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Filed: May 21, 2004	)	
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For: EXPANDABLE STENT AND METHOD FOR DELIVERY OF SAME	) :)	August 21, 2006

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

MISCELLANEOUS INCOMING LETTER-

SUBMISSION OF DOCUMENTS UNDER 37 CFR § 1.97(i)

Sir:

In accordance with 37 CFR § 1.97(i), please place the attached documents in the subject application file.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should continue to be directed to our address as given below.

Respectfully submitted,

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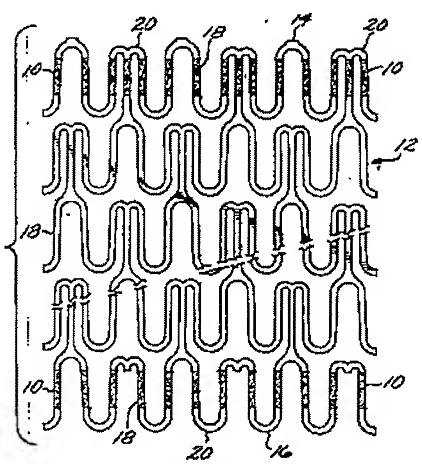
(54) Radiopaque stent markers.

(57) A radiopaque marker associated with a stent which is adapted to be implanted into a body lumen of a patient to maintain the patency thereof and a convenient and accurate method for affixing the radiopaque marker to the stent. The radiopaque marker defining an acceptable profile and capable of facilitating, under fluoroscopy, the identification of the position, diameter and length of a stent without obscuring the lesion being repaired and without impeding the deformation of an expandable stent.

FIG. 1A



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BACKGROUND OF THE INVENTION

This invention relates to endoprosthesis devices, generally called stents, and, more particularly, radiopaque markers for use with endoprosthesis devices.

Stents are useful in the treatment of atherosclerotic stenoses in blood vessels and are generally tubular shaped devices which function to hold open a segment of a blood vessel or other anatomical lumen. They are particularly suitable for use in supporting and holding back a dissected arterial lining which can occlude the fluid passage way therethrough.

In order to accomplish precise placement of stents, various means are employed to identify the position of the stent within a blood vessel. One means frequently described for accomplishing precise placement of a stent is the attachment of radiopaque markers to the stent so that through the use of fluoroscopy, the position of the stent within a blood vessel can be identified. Once the stent with its radiopaque markers has been implanted, subsequent checkups of the treated segment are easily performed since the markers remain visible under fluoroscopy.

Conventional radiopaque markers, however, have various limitations. Upon attachment to a stent, certain conventional radiopaque markers define a profile that is readily discernible from that of the stent, thereby comprising projections which may undesirably alter the contemplated profile of the stent. That is, these conventional radiopaque markers protrude from the walls of the stent and depending upon their location upon the stent, may either project into the blood flow or into the walls of the blood vessel. In addition, these conventional radiopaque markers are limited in that their attachment to the stent can be tedious and imprecise.

Other conventional radiopaque markers restrict the expansion capabilities of an expandable stent by adding rigidity to the stent in areas designated for stent deformation. Still other conventional stents utilize material, such as tantalum, that is effective for use in identifying the location of a stent within a vessel, but fluoroscopically illuminate so brightly so as to obscure proper visibility of the blood vessel lesion, thereby impairing the ability to repair the lesion. Finally, conventional radiopaque markers do not generally, under fluoroscopy, provide the operator with means to accurately assess stent length and diameter.

To overcome the problems and limitations associated with stents having conventional radiopaque markers, it would be desirable to employ radiopaque markers that can be consistently and precisely attached to a stent, that do not limit the expansion capabilities of an expandable stent, that define an acceptable profile, that provide means to assess stent length and diameter and that do not obscure the blood vessel lesion being repaired.

SUMMARY OF THE INVENTION

Particular embodiments of the invention provide a radiopaque marker that may be consistently and precisely affixed to a stent, that does not limit the expansion capabilities of an expandable stent, that has an acceptable profile and that may effectively identify the position, diameter and length of a stent within a blood vessel without obscuring a lesion being repaired. Certain embodiments also provide means for affixing to a stent a radiopaque marker having the aforementioned characteristics.

A radiopaque marker embodying the invention may be utilized with stents having various geometric shapes and materials. In addition, the radiopaque marker may be positioned anywhere on a stent and may comprise any plateable radiopaque material having various patterns. Further, any acceptable means for affixing the radiopaque marker to a stent may be employed. It is preferable, however, that the means for attaching a radiopaque marker, its location upon a stent as well as the material and geometric shape of the stent, be selected so that a stent incorporating the radiopaque marker embodying the invention may benefit from the advantages provided thereby.

In a preferred embodiment, the radiopaque markers of the present invention are affixed to both a distal and a proximal end of a generally cylindrical stent. In this embodiment, the radiopaque marker material is gold and is affixed to the outside circumference of a generally cylindrical stent by means of plating. Although gold is the designated material of this embodiment, other biocompatible plateable radiopaque materials, such as platinum, are equally desirable. Plating is preferable since it can be performed easily and with accuracy and can be utilized to produce an acceptable radiopaque marker profile. It is contemplated that the thickness of the radiopaque marker material upon a stent be in the range of about 0.008 to 0.080 mm (.0003 to .003 inches) on the exterior surface of the stent, and if required for fluoroscopic illumination, the same thickness can be plated to the inner stent surface. It is also contemplated that the stent may comprise any material, for example any metal or plastic, upon which gold may be plated.

Although radiopaque material may be plated on only a portion of the circumference of the stent, in a preferred embodiment it is contemplated that the entire circumference of the stent be plated, thereby producing a stent with a band of radiopaque material at its distal and proximal ends. Moreover, it is significant that only the ends of the stent are plated and that gold, or a similarly effective material, may be selected as the plating material. Plating provides controlled deposition of the radiopaque material on the stent thereby controlling its fluoroscopic illumination. By plating only the two ends of the stent, the fluoroscopic illumination is thus limited to the ends of the stent. These

two features minimize the possibility of obscuring the fluoroscopic visualization of the blood vessel being treated.

In addition, by plating with radiopaque material at both ends and upon the outside of a generally cylindrical stent, not only can the location of the stent be determined under fluoroscopy, but the length and diameter of the device can be determined as well. This is particularly useful where the subject stent is expandable, since the degree of expansion can be ascertained by noting the height of each radiopaque marker and the relative distances between the radiopaque markers. Further, it can be determined under fluoroscopy whether or not the stent is twisted or otherwise improperly seated within a blood vessel.

In order to successfully plate gold, or any acceptable radiopaque marker material upon a stent, the stent is placed upon a mandrel, then is masked and plated. In a preferred procedure, the stent is placed upon an elongated cylindrical mandrel, masked with shrink tubing, portions of which are lased away to expose the areas of the stent desired to be plated and, thereafter, plated with the desired radiopaque material. It is contemplated that the mandrel may comprise annular recesses which function to allow portions of an interior circumference of a stent, as well as the exterior of that stent, to be plated.

Subsequent to the completion of the plating procedure, in a preferred procedure the shrink tubing is detached from the stent and the stent is removed from the mandrel. It is contemplated that the shrink tubing may be cut from the stent utilizing a laser. Alternatively, the shrink tubing may be dissolved with chemicals. It also is contemplated that the shrink tubing be pre-fabricated or cut to size (by means of a laser) to precise dimensions, so that the tubing properly can perform its masking function.

Since a preferred embodiment contemplates gold plating as the avenue for affixing radiopaque markers to a stent, and since gold plating may stiffen a stent in the areas of plating, it is contemplated that expandable stents may be plated in areas where additional rigidity does not affect the expansion capabilities of the stent. Thus, portions of a stent that do not deform upon expansion are plated with gold or the desired radiopaque material. In this way, the stent can freely and uniformly expand and elastically deform without additional restrictions, thereby accomplishing its expansion function while still benefitting from the advantages of the present invention.

In another embodiment, the entire exterior surface of a stent is plated with radiopaque material. Thereafter, the portions designated to retain radiopaque material are masked and the radiopaque material is etched away from the remaining portions of the stent.

In yet another embodiment, a generally cylindrical stent is fitted with radiopaque markers having some geometrical configuration or placed upon a stent in some pattern. For instance, a radiopaque marker may comprise a sine wave pattern so that under fluoroscopy, the configuration of the stent may be quickly ascertained. That is, it can be readily ascertained whether the stent is improperly twisted or contorted and, in the case of an expandable stent, whether the stent properly has been deformed.

Other features and advantages of the present invention will become apparent from the following detailed description, taken in conjunction with the accompanying drawings, which illustrate, by way of example, the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1A illustrates a partial view of a stent embodying radiopaque markers.

FIG. 1B illustrates a partial view of another stent embodying radiopaque markers.

FIG. 2A illustrates a schematic view of a stent embodying radiopaque markers.

FIG. 2B illustrates a schematic view of another stent embodiment having radiopaque markers.

FIG. 3A illustrates a perspective view of a mandrel having annular recesses.

FIG. 3B illustrates a perspective view of a mandrel without annular recesses.

FIG. 4A illustrates a partial cross-sectional view of a masked stent loaded upon a mandrel having annular recesses.

FIG. 4B illustrates a partial cross-sectional view of a masked stent loaded upon a mandrel without annular recesses.

FIG. 5 illustrates a schematic view of the stent having two rows of radiopaque material along the longitudinal axis in addition to the radiopaque material on either end of the stent.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

As is shown in the drawings, which are included for purposes of illustration and not by way of limitation, there is provided a radiopaque marker 10 (FIGS. 1 and 2). Conventional radiopaque markers are limited in that they may comprise undesirable projections extending from a stent, may be arduous to attach, restrict the expansion capabilities of an expandable stent and may be ineffective in the identification of the position, orientation and configuration of a stent. The illustrated radiopaque marker 10 defines an acceptable, very low, profile, conveniently may be affixed to a stent, does not impede the expansion capabilities of an expandable stent, and may be useful in identifying the position, orientation and configuration of a stent within a blood vessel. The illustrated radiopaque marker therefore, provides superior means

of marking a stent.

The illustrated marker facilitates precise placement of a stent 12 by way of its novel configuration, position upon a stent, and material properties. The characteristics of a radiopaque marker 10 are selected to assure that a stent 12 embodying the radiopaque marker 10 may benefit from the advantages which the invention provides. Thus, radiopaque marker 10 may have various geometric shapes, comprise various materials and may be positioned anywhere on a stent 12, so long as the desired advantages of the invention are achieved.

In a preferred embodiment, radiopaque marker 10 is plated upon an outer circumference of a generally cylindrical stent 12 and upon a proximal end 14 and a distal end 16 of the stent 12. In another embodiment, it is contemplated that an inner circumference underlying the outer circumference be plated as well. By utilizing plating as the means for affixing radiopaque marker 10 to a stent 12, a minimum profile may be achieved. It is contemplated that the thickness of radiopaque marker 10 be in the range of about 0.008 to 0.080 mm (.0003 to .003 inches) . As such, the radiopaque marker 10 does not appreciably alter the profile of stent 12 and therefore, does not result in stent 12 having substantial projections extending into the blood flow or into the walls of the blood vessel being repaired.

In addition, by plating or similarly affixing radiopaque material upon a stent, radiopaque markers 10 easily and accurately can be affixed to a stent. That is, plating is an improved means of affixing radiopaque material to stent 12 over conventional means of affixing radiopaque markers, such as sewing or bonding, which can be tedious and imprecise.

Although it is not necessary for all embodiments, the preferred embodiment contemplates that the entire circumference of the stent be plated at both its proximal end 14 and distal end 16. It is also contemplated that the plating material may be gold or a material, such as platinum, which has similar radiopaque characteristics .

It is significant that gold, or a similar material, is contemplated as the preferred radiopaque marker material. Other metals suitable as radiopaque markers include, for example, platinum and silver. By selecting such a material, the stent may be effectively identified under fluoroscopy. In various conventional stents, the radiopaque material employed glows so brightly under fluoroscopy so as to obscure the lesion being repaired. In contrast, the images of radiopaque markers comprised of gold or platinum do not, under fluoroscopy, substantially obscure the lesion being repaired.

It is also significant that the preferred embodiment contemplates affixing radiopaque markers 10 to the ends of stents 12 having various geometric configurations (see FIGS. 2A and 2B). By doing so, the orientation or configuration of the stent 12, irrespective of its geometric configuration, can be ascertained, which is particularly important to the determination of whether a stent has completely repaired a blood vessel. By noting the distance between the radiopaque bands, the length of the stent 12 can be ascertained and compared to an expected stent length. By observing the height or width of the radiopaque markers 10, the extent of expansion of an expandable stent 12 can be ascertained and compared with expected values. Similarly, by examining the radiopaque markers embodying the invention under fluoroscopy, it can be determined whether the stent 12 is twisted or otherwise improperly is seated within a vessel.

The plating of radiopaque markers upon a stent may add some rigidity to a stent in the areas of plating. Since this is the case, the preferred embodiment contemplates affixing radiopaque markers 10 to only those portions of an expandable stent 12 that do not deform upon expansion. As shown in FIGS. 1a and 1b for example, radiopaque markers 10 may be affixed to straight segments 18 of the proximal end 14 and distal end 16 of a stent. Upon expansion, the curved portions 20 of the stent 12 may deform so as to allow the stent 12 to expand, while the straight portions 18 may remain undeformed. By affixing radiopaque markers 10 to the straight portions 18 of stent 12 as shown in FIGS. 1A and 1B, the additional rigidity added to the stent 12 by the radiopaque markers 10 does not impede expansion. Therefore, an expandable stent having radiopaque markers 10 embodying the invention can expand uniformly and predictably.

In order to plate a radiopaque marker 10 upon a stent 12, a mandrel 30 may be employed (see FIG. 3A) . The mandrel 30 may comprise any suitable material formed into an elongate cylindrical shape having a main portion 21 with a cross-sectional diameter sized for receiving stent 12. The mandrel may further embody a collar 22 formed or attached to one end of the mandrel 30 that has a cross-sectional diameter larger than that of stent 12 and two annular recesses 23 formed in the main portion 21 which have cross-sectional diameters less than that of the main portion 21. The collar 22 functions as a stop and may aid in registering stent 12 upon the mandrel 30. Annular recesses 23 function to allow interior surfaces of stent 12 to be plated. In another embodiment of mandrel 30 (FIG. 3B), recesses 23 may be sufficiently shallow or be missing entirely from mandrel 30 so that, where desirable, interior surfaces of stent 12 are not plated with radiopaque material.

In a preferred method, stent 12 is placed upon mandrel 30 and heat shrink tubing 32 (see FIGS. 4A and 4B) is slipped over stent 12. The heat shrink tubing 32 is then exposed to heat to shrink the tubing on the stent 12. It is contemplated that the heat be concentrated at a midpoint of the heat shrink tubing 32

and then gradually apply heat towards each end so as to prevent distortion of the stent. The shrink tubing 32 may be any polyester having heat shrink properties and the ability to mask the stent during the electroplating process.

Once the heat shrink tubing 32 is snug upon stent 12, the stent may be precisely positioned on the mandrel 30 and then temporarily secured in place using a high temperature wax. Where it is desired to plate an interior as well as an exterior surface of stent 12, the annular recesses 23 may be aligned with the interior portions of the stent 12 desired to be plated (see FIG. 4A). Where it is deemed undesirable to plate the interior surface, no such further alignment is necessary (see FIG. 4B). Next, the curved portions 20 (Fig. 1B) of stent 12 as well as the ends of the mandrel 30 can be dipped in high temperature wax to prevent them from being plated.

In order to plate the desired portions of stent 12, the heat shrink tubing 32 surrounding portions of the stent 12 to be plated may be cut away using a standard CO_2 laser or its equivalent. The laser output is to be limited so that stent 12 and mandrel 30 are not affected. By utilizing a mandrel 30 without annular recesses (see FIGS. 3B and 4B), portions of the heat shrink tubing 32 may be lased away so that only the outer circumferences of stent 12 may be plated. By employing the mandrel 30 illustrated in FIGS. 3A and 4A, portions of the heat shrink tubing 32 overlaying annular recesses 23 may be lased away, thereby resulting in a stent 12 having desired portions of its interior as well as its exterior plated with radiopaque material (see FIG. 2B).

As with any electroplating process, an electrical current is used in the process of putting a metallic coating on a metal or other conducting surface. In the preferred embodiment, a gold solution exists in the form of positively charged ions that have lost one or more electrons. The stent is connected to the cathode or negative terminal and the anode, or positive electric terminal, is connected to the stainless steel mandrel 30 which is dipped into the gold solution. The ions are attracted to the cathode and the coating is deposited on the stent metal surface. As is known in the art, the thickness of the layer deposited depends on the amperage of the electric current, the concentration of the metallic ions and the length of time that the stent is plated. The plating process should be at a low enough amperage to prevent mapping, nodules, or a matte surface.

After plating the gold on the stent, the wax is removed from stent 12 and mandrel 30 by inserting the two elements into acetone or an equivalent solution.

As can be appreciated from the drawings (FIGS. 2A and 2B), the end portions 36,38 of a stent 12 which are not masked, are plated with radiopaque material and the portions of the stent 12 which are masked, are not plated.

Once the stent 12 is plated with a radiopaque marker 10, it is removed from the mandrel 30 and the heat shrink tubing 24 is stripped away. The heat shrink tubing 24 may be removed, for example, by cutting it with a laser or in the alternative, dissolved with chemicals. Finally, the mandrel 30 is withdrawn from the plated stent 12 and the stent 12 may be cleaned with an alcohol-containing solution such as "Alcomox," or equivalent solution.

In another embodiment, the entire exterior surface of a stent may be plated with radiopaque material. Subsequent to plating, the stent 12 is masked and subjected to etching. In this embodiment, the areas designated to retain radiopaque material are masked and the radiopaque material is etched away from the remaining portions of the stent.

In yet another embodiment, radiopaque markers having some pattern are affixed to a generally cylindrical stent so as to facilitate the identification, position and configuration of a stent 12 within a blood vessel. For example, the pattern of a radiopaque marker 10 may be in the form of a sine wave. As the sine wave expands along with the stent during deployment, it is visible under fluoroscopy and it can be determined whether the stent 12 is properly seated within a blood vessel by viewing the amplitude and shape of the sine wave radiopaque marker. As another example, as depicted in Fig. 5, the pattern 13 of a radiopaque marker 10 may be a continuous or dashed line extending from the proximal end 14 to the distal end 16 of stent 12. A longitudinal marker of the type described will allow the doctor to determine if the stent has twisted upon deployment or if it expanded unevenly.

In an alternative embodiment, a radiopaque plastic may be coated or affixed to all or a portion of a stent. In this embodiment, a radiopaque plastic is formed by loading a plastic material with a radiopaque material such as barium sulfate or bismute trioxide. The resultant mixture is then coated or affixed to the stent. Several methods of affixing the radiopaque material to the stent are contemplated and include: (1) melting the radiopaque material and then dipping the stent into the melt; (2) solvent casting; and (3) vacuum deposition. These methods are known generally and various process steps are apparent to those skilled in the art. As with the plating process steps described above, the stent can be masked and mounted on a mandrel and then coated, by dipping, solvent casting, or vacuum deposition.

From the foregoing it will be appreciated that the radiopaque marker described effectively identifies the location and configuration of a stent within a patient's body lumen of a patient and provides a method and apparatus for constructing the same.

While several particular forms of the invention have been illustrated and described, it will also be apparent that various modifications can be made without departing from the scope of the invention. Thus,

it should be understood that various changes in form, and detail, and application of the present invention may be made without departing from the scope of this invention.

Claims

1. A radiopaque marker (10), comprising: a band of radiopaque material affixed by means of plating to at least a portion of an outer circumference of a generally cylindrical stent (12).

2. The radiopaque marker (10) of claim 1, wherein said radiopaque marker is affixed adjacent a proximal end (14) and a distal end (16) of the generally cylindrical stent (12).

3. The radiopaque marker (10) of claim 1, or claim 2 wherein said stent (12) is expandable and comprises a deforming portion (20) and a non-deforming portion (18), the radiopaque marker being affixed to said non-deforming portion (18).

4. The radiopaque marker (10) of any preceding claim, wherein said radiopaque material comprises a metal taken from the group of gold, platinum and silver.

5. The radiopaque marker (10) of any preceding claim, wherein said band of radiopaque material has a thickness in the range of approximately 0.008 to 0.080 mm (.0003 to .003 inches).

6. The radiopaque marker (10) of any preceding claim, wherein said band extends a full circumference of a portion of said stent (12).

7. The radiopaque marker of any preceding claim, wherein said band comprises a pattern (13).

8. The radiopaque marker (10) of claim 7, wherein said pattern (13) comprises a wave-like shape.

9. A medical device for implantation in a blood vessel or artery, comprising:
   an intravascular stent (12) having a generally cylindrical configuration; and
   a radiopaque material (10) affixed to a portion of said intravascular stent so that said radiopaque material (10) is visible under fluoroscopy and can be easily located in the blood vessel or artery where said stent (12) is being implanted.

10. The medical device of claim 9, wherein said intravascular stent (12) has a proximal end (14) and a distal end (16) and said radiopaque material (10) is coated adjacent said proximal end (14) and said distal end (16).

11. The medical device of claim 9, or claim 10 wherein said stent (12) is expandable and comprises a deforming portion (20) and a non-deforming portion (18), and said radiopaque material (10) is affixed to said non-deforming portion (18).

12. The medical device of any of claims 9 to 11, wherein said radiopaque material (10) comprises a metal taken from the group of metals consisting of gold, platinum and silver.

13. The medical device of any of claims 9 to 12, wherein said radiopaque material (10) has a thickness in the range of approximately 0.008 to 0.080 mm (.0003 to .003 inches).

14. The medical device of any of claims 9 to 13, wherein said radiopaque material (10) extends a full circumference of a portion of said stent (12).

15. The medical device of any of claims 9 to 14, wherein said radiopaque material comprises a pattern (13).

16. The medical device of claim 15, wherein said pattern of said radiopaque material comprises a wave-like shape.

17. A method for affixing a radiopaque marker to a generally cylindrical stent (12) comprising the steps:
   placing said stent (12) upon a mandrel (30);
   attaching masking material (32) to a portion of said stent (12);
   coating at least a portion of said stent (12) with a radiopaque material;
   removing said masking material (32) from said stent; and
   removing said stent (12) from said mandrel (30).

18. The method of claim 17, wherein said masking material (32) is a heat shrink tubing, which is heated and applied to a portion of said stent (12).

19. The method of claim 17 or claim 18, wherein said coating step includes plating a coating of metal on a portion of said stent (12), the metal taken from the group gold, platinum and silver.

20. The method of any of claims 17 to 19, wherein said coating step includes coating a radiopaque plastic on a portion of said stent.

21. The method of any of claims 17 to 20, wherein

said coating step includes dipping said stent (12) in a solution of radiopaque plastic so that said portion of said stent receives said coating of radiopaque plastic.

22. The method of any of claims 17 to 21, wherein said coating step includes solvent casting a radiopaque plastic on at least said portion of said stent (12).

23. The method of any of claims 17 to 22, wherein said coating step includes vacuum deposition of a radiopaque plastic on at least said portion of said stent (12).

24. The method of any of claims 17 to 23, wherein said masking material (32) is pre-fabricated to pre-determined dimensions.

25. The method of any of claims 17 to 24, wherein said masking material (32) is cut to desired dimensions once placed upon said stent (12).

26. The method of claim 25, wherein said masking material (32) is cut to desired dimensions by use of a laser.

27. The method of any of claims 17 to 26, wherein said masking material (32) is removed by using a laser to cut said masking material from said stent (12).

28. The method of any of claims 17 to 27, wherein said masking material (32) is removed by dissolving said masking material with chemicals.

29. A method for affixing a radiopaque marker (10) to a generally cylindrical stent (12) comprising the steps:

placing said stent upon a mandrel (30);

plating said stent with a radiopaque material;

masking a portion of said stent with a masking material (32);

etching said radiopaque material from an unmasked portion of said stent; and

removing said masking material from said stent.

30. The method of claim 29, wherein said plating step includes depositing a coating of metal on a portion of said stent, said metal taken from the group gold, platinum and silver.

31. The method of claim 29 or claim 30, wherein said plating step includes depositing a coating of a radiopaque material on a portion of said stent (12).

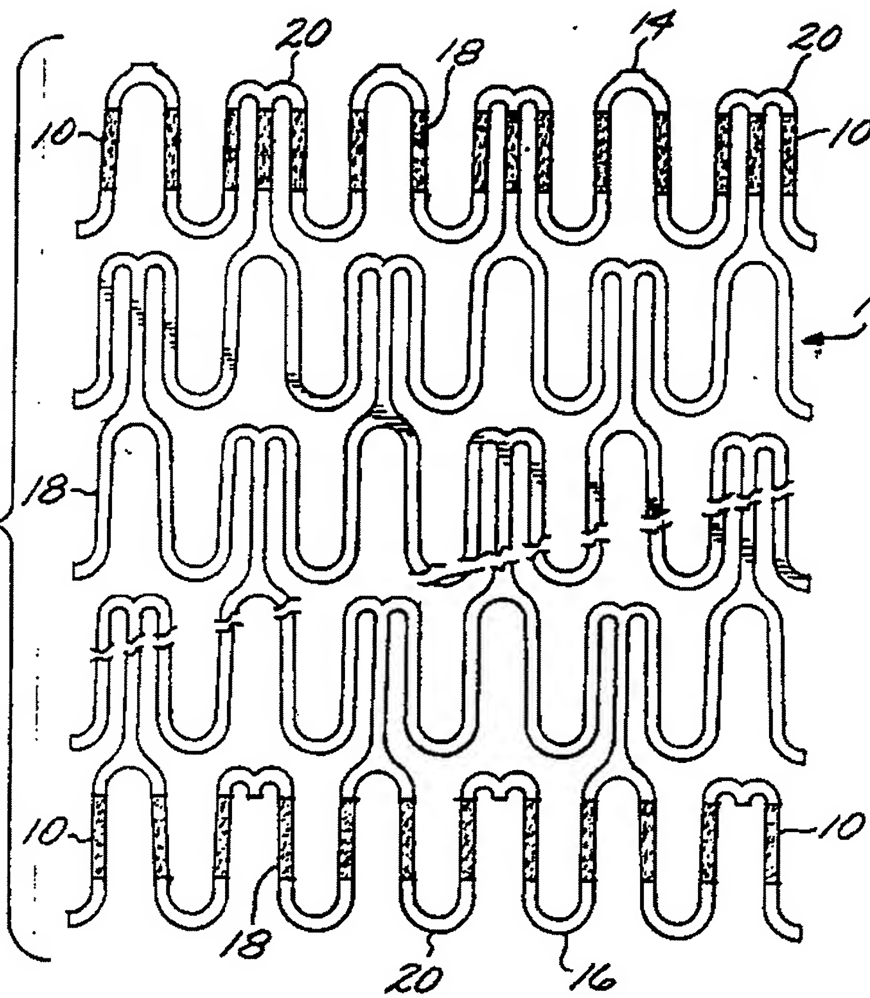


FIG. 1A

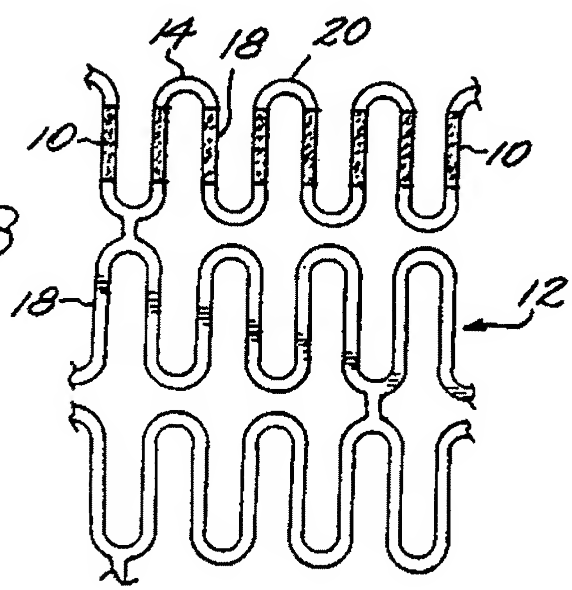


FIG. 1B

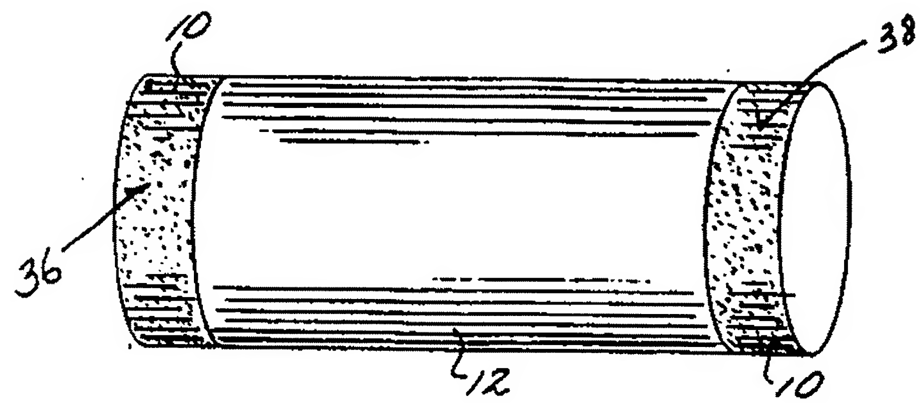


FIG. 2A

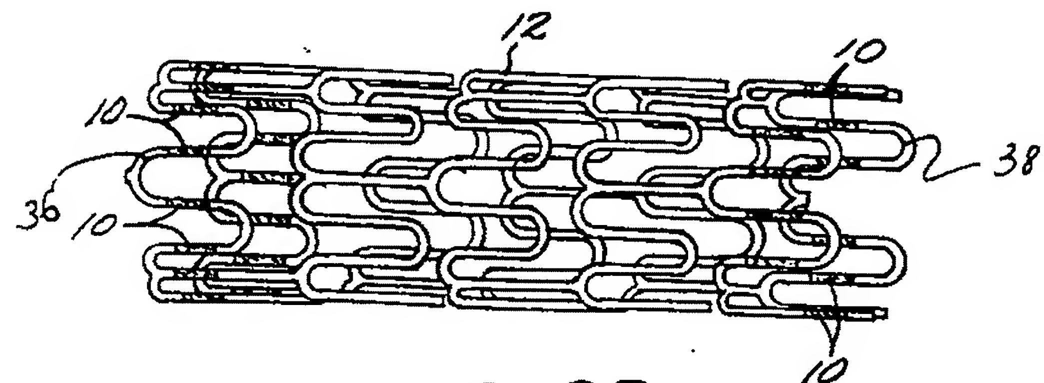


FIG. 2B

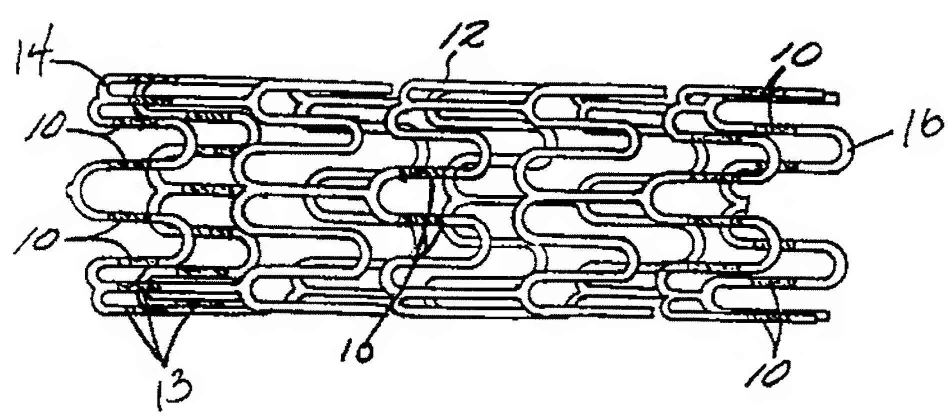


FIG. 5

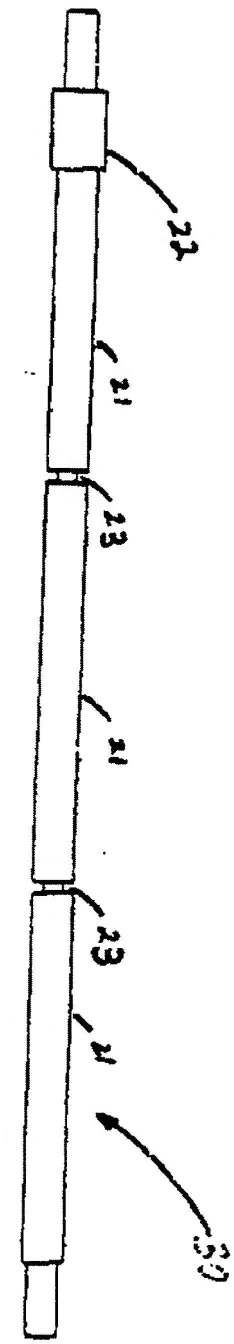


FIG. 3A

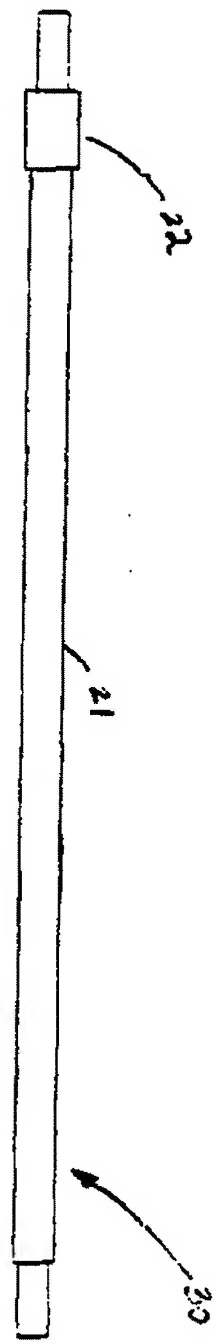


FIG. 3B

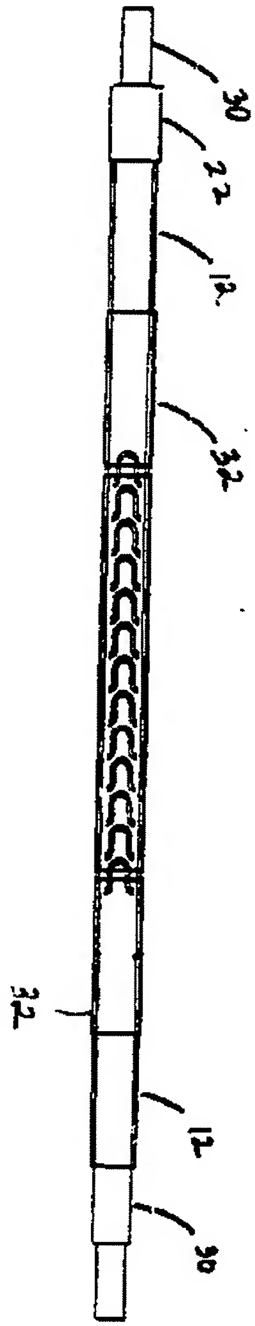


FIG. 4B

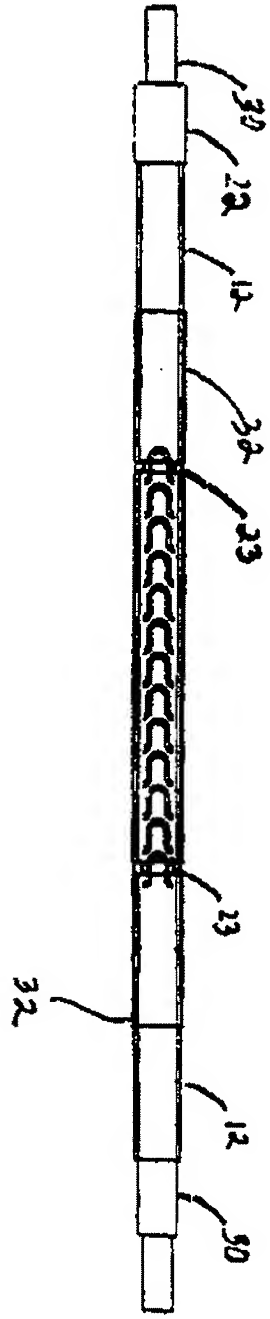
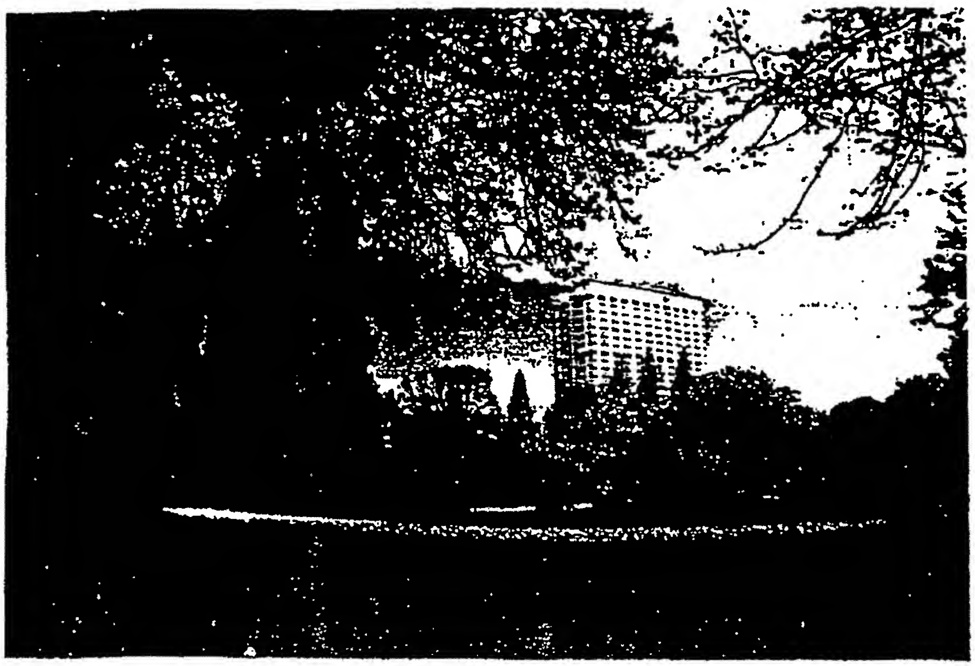


FIG. 4A

SECOND THORAXCENTER COURSE ON CORONARY STENTING



Rotterdam, The Netherlands

December 13-16, 1995

Course Programme

Wednesday December 13

12.00-13.30	Registration with lunch	

Opening Address:

13.30-13.35	Marcel van den Brand	

Session: History

13.35-13.45	Lessons learned from the past	Richard Schatz
13.45-14.00	First stent course cases revisited	Peter Ruygrok

Template Session: The second generation of the old and the first generation of the new

Technical anchorman: Marcel van den Brand

Chairmen: Richard Schatz and Peter Ruygrok

The commercially available stents

14.00-14.05	Less shortening Wallstent and uni-step delivery	JeanMarco
14.05-14.10	Low profile Gianturco-Roubin stent	Gary Roubin
14.10-14.15	Palmaz-Schatz stent with spiral bridge	Richard Schatz
14.15-14.20	Wiktor stent monorail and short wave	Christopher White
14.20-14.25	AVE stent new configuration	Simon Stertzer
14.25-14.30	ACS Multilink	Ulrich Sigwart

14.35-16.05	Live cases 1 and 2	

Pilot and registry phase

16.05-16.10	Cordis	Martin Rothman
16.10-16.15	SciMED	Robert Schwartz
16.15-16.20	Angiostent	Ziyad Hijazi
16.20-16.25	Instent	Rafaël Beyar
16.25-16.30	Freedom	Ivan De Scheerder
16.30-16.35	Act-One	Frank Litvack
16.30-17.00	Tea break	

Pre-clinical

17.00-17.05	STS stent	Ivan De Scheerder
17.05-17.10	Biotronic stent	Hans Bonnier
17.10-17.15	NIR stent	Yaron Almagor
17.15-17.20	EB stent	Enzo Borghi

17.20-18.00 Cross fire:

So many stents: Necessity or marketing?

Chairman: Professor Paul Hugenholtz, Past President of the European Society of Cardiology

Panel: Bas de Mol, Cardiothoracic surgeon, AMC, Amsterdam

Marvin Woodall, President Johnson & Johnson Interventional Systems

Marcel van den Brand, Cardiologist, Thoraxcenter, Rotterdam

Thursday December 14

Technical anchorman: Marcel van den Brand

	Stent related problems	
	Subacute thrombosis: A local or systemic problem ?	
	Chairmen: Stephen Ellis and Maarten Simoons	
08.00-08.15	"Hemostaseological" predictors of stent thrombosis	Franz-Josef Neumann
08.15-08.30	Pharmacological interaction	Luisa Gregorine
08.30-08.45	Heparin coated stents. In vivo angioscopic insights	Giulio Guagliumi
08.45-09.00	GPIIB/IIIA antagonists: a new actor in stenting	Stephen Ellis
09.00-09.15	Experimental data on heparin coated stent	Anthony Lum
09.15-09.30	The next generation of stent coatings	Nicolas Chronos
09.30-11.00	Live cases 3 and 4	
11.00-11.30	Coffee break	
	Restenosis within the stent	
	Chairmen: Joseph Carrozza and Wim van der Giessen	
11.30-11.50	The Emory view	Neal Scott
11.50-12.10	The Mayo view	Robert Schwartz
12.10-12.30	Practical implications: The Emory and Mayo viewpoints	Spencer King III and David Holmes
12.30-12.50	Treatment of restenosis within the stent	Joseph Carrozza
12.50-14.30	Lunch	
13.30-14.15	Live satellite transmission from Birmingham Alabama, USA Stenting of Carotid artery stenosis - Gary Roubin	
14.30-15.30	Live case 5	

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Session : Cost effectiveness

Chairmen: David Cohen and Jelle Braaksma

15.30-15.40	Cost effectiveness of the Benestent study	Ben van Hout
15.40-15.50	Cost effectiveness of the radial approach	Ferdinand Kiemeneij
15.50-16.00	Cost effectiveness of the STRESS I study	David Cohen
16.00-16.05	Concluding remarks	Jelle Braaksma
16.05-16.35	Tea break	
16.35-18.00	Live cases 6 and 7	
18.30..	Cocktail party Sponsored by Schneider AG	

Friday December 15

Technical anchorman: Peter de Jaegere

Session: Randomized trials and Registries

Chairmen: Eugène McFadden and Patrick Serruys

08.00-08.10	Meta analysis of Benestent I and Stress I and II	Alda Azar
08.10-08.20	Benestent II pilot	Hakan Emanuelsson
08.20-08.30	Rest study	Raimund Erbel
08.30-08.40	Stent-by	Michael Haude
08.40-08.50	GRACE	Eugène McFadden
08.50-09.00	SAVED	Michael Savage
09.00-10.30	Live cases 8 and 9	
10.30-11.00	Coffee Break	

Chairmen: Marie-Claude Morice and Jeffrey Popma

Technical anchorman: Peter de Jaegere

11.00-11.10	RAVES	Jeffrey Popma
11.10-11.20	TASC II	Ian Penn
11.20-11.30	Strut non-randomized	Peter Fitzgerald
11.30-11.40	MUSIC	Peter de Jaegere
11.40-13.10	Live cases 10 and 11	
13.10-14.40	Lunch	

Chairmen: Jeffrey Popma and Marie-Claude Morice

14.40-14.50	MUST	Marie-Claude Morice
14.50-15.00	START	Antonio Serra
15.00-15.10	WEST	Keith Dawkins
15.10-15.20	Access	Ferdinand Kiemeneij

Session: Guided stent implantation

Chairmen: Carlo Di Mario and Jos Roelandt

15.20-15.35	Is there a place for physiologic assessment?	Carlo Di Mario
15.35-15.50	QCA on-line for stenting: a neglected gold standard or the poor man's IVUS?	David Foley
15.50-16.05	IVUS guided stenting	Gary Mintz
16.05-16.20	EBT: New imaging technique for stenting	Raimund Erbel
16.20-16.50	Tea break	
16.50-17.50	Live case 12	
19.00-22.00	Social event	

Saturday December 16

Session: Stent of the future

Chairmen: Spencer King III and Wim van der Giessen

08.00-08.15	Follow-up of the Glastra stent	Wim van der Giessen
08.15-08.25	Drug delivery stent what's new?	Richard Stack
08.25-08.35	Drug-loaded stent: effect on thrombogenicity and restenosis	Ivan De Scheerder
08.35-08.40	Discussion	
08.40-08.50	Radioactive stenting - European view	Christopher Hehrlein
08.50-09.00	Radioactive stenting - American view	Tim Fischell
09.00-09.05	Discussion	
09.05-09.15	Catheter based endovascular radiation	Spencer King III
09.15-09.25	First clinical experience with endovascular radiation post stenting	Paul Teirstein
09.25-09.30	Discussion	
09.30-09.40	Vein covered stenting - European view	Chris Stefanides
09.40-09.50	Vein covered stenting - American view	Bill O'Neill
09.50-09.55	Discussion	
10.00-10.30	Coffee break	

Session: Expanding the envelope

Chairmen: Martin Leon and Lex van Herwerden

10.30-10.40	Synergy: necessity or extravagance	Martin Leon
10.40-10.50	Main stem lesion/bifurcation lesion	Antonio Colombo
10.50-11.00	Total reconstruction Wallstent	Patrick Serruys
11.00-11.10	Carotid stent	Gary Roubin
11.10-11.20	Graft stent (conduit)	Richard Heuser
11.20-11.30	Aortic stent graft	Juan Parodi
11.30-11.40	Stenting in acute myocardial infarction	Marie-Claude Morice
11.40-11.50	Bail-out stenting in acute myocardial infarction and antithrombotic therapy	Albert Schömig
11.50-12.40	"Bleeps, blunders and bloopers": confessions on video	

12.40-13.15 Presentation of the Erasmus Thoraxcenter Interventional Cardiology Award (ETHICA)
Patrick Serruys and Pim de Feyter

Nominees and awardees for:
Best inventor of the year 1995
Best experimental researcher of the year 1995
Best clinical researcher of the year 1995

Closing remarks: Pim de Feyter

The Practice of Interventional Cardiology

Second Edition

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Stents for Bailout and Restenosis

Spencer B. King III, M.D.

The mechanism of coronary angioplasty is expansion of the constricted arterial lumen to produce cracks in the intima, various degrees of splits into the media, and often separation of the plaque from the vessel wall. After the balloon is deflated and removed, the arterial pressure keeps the artery open, but some recoil of the tissues results in a lumen that is consistently smaller than the inflated balloon. On average that recoil amounts to about 30% of the diameter or 50% of the cross-sectional area. Closure of coronary arteries after angioplasty is obviously multifactorial, but the decreased lumen just after balloon deflation may play a role in both acute closure and late restenosis.

The concept of intracoronary stenting arises from a recognized need in some cases to counter this elastic recoil phenomenon and to reattach these separated plaque segments. If a prosthetic device is placed in the artery after balloon deflation, then the vessel may be held open to the same size as the balloon and the adjacent unobstructed artery. By leaving a larger lumen, the chance of early reclosure and late restenosis may be minimized. Some arteries are so severely dissected that acute occlusion immediately after angioplasty occurs. In those cases, dissected intimal flaps can be reapproximated to result in a restored functional lumen. Another mechanism by which stents are advantageous is by creating smoother walls of the dilated artery. The irregular geometry created by plaque fissuring and separation from the vessel wall is a perfect substrate for platelet deposition and thrombus formation.[1] Chesebro et al. have shown a direct correlation between the extent of injury and the amount of platelet deposition.[2] Stenting, by the mechanism of sealing flaps and cracks, creates a smoother inner surface of the lumen. Whether these beneficial effects of stenting, i.e., providing a wide and smoother lumen, will translate into a reduced risk of acute closure and late restenosis has been the subject of ongoing stent investigations. In this chapter, I will describe some of the background experimental work on stenting, the various stent designs that are under investigation, the use of stents in the setting of acute closure, the potential for stents to reduce the rate of restenosis, and the future for stents as a local drug delivery system.

EXPERIMENTAL TESTING

Animal testing of stents has been instructive but has left more questions unanswered than answered. As early as the late 1960s, Dotter was placing wire coil grafts in dog femoral arteries and assessing long-term patency.[3] More recently the Palmaz-Schatz stent[4] and the Gianturco-Roubin stent[5] have been evaluated in dog coronary arteries. The healing phenomenon is very consistent and limited. Within a few days, cells resembling endothelial cells begin to cover the stent wires, and within 2 weeks there is a confluent covering. The neoendothelial lining thickens until about 8 weeks, reaches a maximal thickness of about 200 to 400 μm, and then begins to regress. Dog coronary arteries examined as late as 2 years show a thin covering over the stent.

Hypercholesterolemic rabbits with stents placed in the iliac arteries developed atherosclerosis internal and external to the stent.[6] At 1 month even though there was extensive atherosclerosis in the stented segment, the lumen of the stented iliac arteries retained greater patency than did the dilated but not stented control iliac arteries.

The pig coronary model has been used by the group at the Mayo Clinic and our group at Emory to test the balloon overstretch plus stent placement in an effort to duplicate the situation encountered in human angioplasty.[7,8] These injured pig arteries sustained significant damage, and the healing process produces extensive proliferation within the stent. Thrombosis in the

stented segment is a problem, and arteries harvested 4 hours after stent placement showed extensive thrombosis. It is felt that this normolipemic pig coronary model may be the best nonprimate model in which to test new strategies for successful stent placement.

TYPES OF STENTS UNDER INVESTIGATION

It is unclear whether the design of stents is of importance in achieving the results desired. Nonetheless, there are significant differences among stent designs. At the present time, more than 20 different stent designs have been proposed. The Medinvent stent is a self-expanding mesh that resembles a Chinese finger splint. In the relaxed state it is expanded. When pulled from the ends, it constricts in diameter and remains constrained by a covering membrane. When the membrane is removed, the stent is released and expands to the size of the artery in which it is deployed. The Palmaz-Schatz stent is composed of a cylindrical stainless steel tube with slots cut so that when it is expanded by a balloon it is deformed into a diamond-shaped matrix. The balloon expansion of the metal device overcomes any elastic component in the metal so that the stent remains deformed in the expanded state. Other balloon-expandable stents are made of stainless steel wire similar to suture material. The Cook (Gianturco-Roubin), Medtronic (Wiktor), and Cordis stents are examples of various coil configurations. Another stent by Boston Scientific (Strecker) is a wire mesh design. All these stents have the ability to perform a scaffolding function; however, there are differences. The Medinvent and Palmaz-Schatz stents provide the smoothest angiographic appearance of the dilated artery. The coil stents have wider interstices, and therefore some dimpling occurs in the vessel wall at the site of each wire loop. The coil stents have, on the other hand, excellent flexibility and can therefore be placed in arteries around moderate curves. Whether flexibility after placement, as is possible with the coil or mesh stents or a rigid artery segment as occurs with the Palmaz-Schatz stent, is important for long-term patency is unresolved.

STENTS AS BAILOUT DEVICES FOLLOWING FAILED ANGIOPLASTY

The most obvious use of stent technology is for the acutely dissected and obstructed coronary artery. The Medinvent, Palmaz-Schatz, and Cook stents have been used for this indication. Closure of coronary arteries following angioplasty occurred in 6.8% of patients treated in the National Heart, Lung and Blood Institute (NHLBI) registry in 1985 and 1986.[9] These patients who suffered acute closure had a five times greater mortality risk and a 27% risk of acute myocardial infarction. Most of these patients, of course, required urgent bypass surgery. Traditional therapy for acute closure has included repeat balloon inflations and prolonged balloon inflations, sometimes using perfusion balloons. If these measures fail, the usual approach to such patients, namely, emergency bypass surgery, has in the past been effective. The low mortality rate in such patients reported earlier by our group[10] has been difficult to maintain in more complex patients undergoing angioplasty. Placement of intracoronary stents in this setting is designed either as a bailout procedure to relieve the acute ischemia and move the patient to bypass surgery or for a more permanent restoration of flow.

The Medinvent stent was utilized for acute closure in 14 of 105 patients receiving the stent in the early experience.[11] In a separate report,[12] the results of stenting for acute closure were detailed; however, most of these patients (13) underwent subsequent early bypass surgery on a semielective basis.

Our major experience with stenting in the setting of acute closure is with the Gianturco-Roubin (Cook) stent. This balloon-expandable stainless steel coil stent had been tested extensively in our institution in animal models and seemed to be well tolerated. We began investigations in the fall of 1987 with a pilot study to assess the ability of the stent to open the artery. In this protocol, the patients were all taken to bypass surgery following stent placement.[13, 14] This experience showed that ischemia could be remarkably reversed by stent placement, that the angiographic lumen could be reestablished, and that normal angiographic flow could be reestablished predictably.

Subsequently a protocol was approved for stent placement in the setting of an acutely disrupted artery in which surgery was not mandated but was left to the discretion of the operator. By utilizing this protocol between September 1988 and December 1990, 100 stents were placed in 93 patients.[15] Patients included were those with complete occlusion at the time of or shortly following angioplasty that could not be resolved with repeat balloon inflations or evidence for imminent closure that consisted of severe dissections or intraluminal plaque that compromised greater than 50% of the lumen and could not be resolved with repeated balloon inflations. The decision to move to bypass surgery rested with the perceived consequence of recurrent arterial closure. Arteries supplying small areas of myocardium were suitable for continued observation of the stent without surgery, as were large arteries supplying

critical areas of myocardium if good collateral systems feeding the distal segment existed. Relative exclusions to stenting were diffusely diseased arteries, multiple lesions in the same artery, the presence of triple-vessel disease, or significant impairment in left ventricular function, as well as akinetic contralateral ventricular wall motion. The smallest stent size available was 2.5 mm, and therefore segments smaller than this as well as segments involving severe bends or branch points that precluded stent placement were avoided. Contraindications to anticoagulation or antiplatelet therapy as well as obvious thrombus formation in the area to be stented were also exclusions.

Stent placement was accompanied by preprocedural therapies of aspirin, intravenous heparin, and calcium channel blocking agents plus dipyridamole, 75 mg, dextran 40 at a rate of 100 mL/hr, and intracoronary nitroglycerin. The dextran was continued at a rate of 100 mL/hr throughout stent placement and then reduced to 50 mL/hr until 500 mL had been administered. More recently, longer infusions of dextran have been advocated. Stents were selected to be slightly larger than the estimated diameter of the artery since this stent design exhibits slight elastic recoil. Additional heparin was given liberally at least every hour during the procedure, and following the procedure a continuous heparin infusion at approximately 1,000 units/hr was begun. Some sheaths were removed the same day after a temporary discontinuation of the heparin to allow the activated clotting time to decline to 150 seconds. Other patients received continuous heparin infusion without interruption until the next day that the sheaths were removed. Following sheath removal a bolus of heparin (2,000 to 5,000 units) and continued infusion were instituted and continued for 3 to 5 days. Further drug therapy included warfarin (Coumadin) adjusted to raise the prothrombin time to 1.5 to 2 times control; aspirin, 80 mg/day; dipyridamole, 75 mg three times a day; diltiazem (Cardizem), 60 mg 4 times a day; and a transdermal nitroglycerin patch. Creatine kinase concentrations and electrocardiograms were obtained serially, and the patients were typically discharged on the fifth day following stenting unless complications occurred.

One hundred two patients with acute closure or threatened acute closure underwent attempted stenting; 109 stents were used in 104 percutaneous transluminal coronary angioplasty (PTCA) procedures. In 9 patients, stents could not be deployed because of an inability to pass the stent through the guiding catheter or through the stenosis itself. All these were removed without losing any stents into the circulation. Ninety-three patients were therefore stented and their results evaluated. Ninety of the 93 stent placements were angiographically successful, that is, they reduced the diameter of the stenosis by greater than 50%. Three patients had successful stent placement, but angiographically the artery was not opened to this degree. Eighty-five of the placements were carried out in native arteries and 10 in saphenous vein grafts. Some characteristics of the stented patients included age, 57 ± 11 years; male, 79%; unstable angina, 79%; class III or IV angina, 73%; prior myocardial infarction, 33%; multivessel coronary disease, 43%; ejection fraction, 56 ± 13% and restenotic lesions, 44%. Some stent placements followed the use of other new technologies. Two patients had atherectomy, 6 had excimer laser therapy, and 7 had laser balloon angioplasty in attempts to solve their acute closure syndrome. The quantitative angiographic stenosis prior to stenting averaged 67%, and following stent placement it was 16%. Relief of ischemia was documented by the fact that of the 58 patients with angina just prior to stent placement, 51 had their angina relieved, and of the 57 patients with ST elevation prior to stenting, 46 patients had resolution of their ST segments to baseline.

Despite successful stent placement in these patients with acute occlusion, complications were relatively frequent. There were 5 deaths, 2 of which seemed unrelated to the stent placement. One had surgery and postoperative peptic ulcer disease with perforation and expired 2 months after the procedure without evidence of ischemia. Another patient suffering left main occlusion during diagnostic catheterization had a stent placed following a prolonged attempt at cardiopulmonary resuscitation; however myocardial function could not be reestablished. One patient with severe chronic obstructive pulmonary disease vomited and aspirated in the poststent follow-up period and sustained a cardiac arrest. The stent was found to be patent and thrombus free at the time of autopsy. Two patients, however, died either as a result of stent placement or because of complications of the antithrombotic therapy. One, who received two stents in the right coronary artery and went to bypass surgery because of severe hypotension documented when total occlusion was present, suffered sudden cardiogenic shock following postoperative protamine reversal. Although no autopsy was obtained, it was speculated that stent thrombosis occurred. Another patient suffered a fatal stroke several days following stenting while receiving heparin. This was assumed to be due to intracranial hemorrhage. In-hospital surgery was performed in 18.9%, Q wave myocardial infarction occurred in 5.2%, repeat PTCA in 5.2%, and subacute closure after the stenting procedure in 7.3%. Sixty-seven patients, or 74%, had none of these complications following stent placement. The other major problems were related to the femoral puncture site. Because of

continued anticoagulation in a rather vigorous manner, femoral artery hematoma occurred in 33%, and pseudoaneurysm repair was required in 8%. During a 14-month follow-up period there have been 2 additional deaths, 1 from acute respiratory failure and 1 following bypass surgery. Bypass surgery was subsequently required in 11 patients, 2 patients suffered Q wave myocardial infarction, and 15 patients had repeat angioplasty.

Although restenosis was not the subject of this trial, angiographic follow-up postdischarge was obtained in 50 patients when they became eligible for a 6-month restudy. This represented 82% of the patients eligible for restudy (that is, those who did not have early bypass surgery). Of the 50 patients restudied, 25 had restenosis defined by 50% or greater diameter reduction. Restenosis was somewhat higher in the circumflex artery (79%) or in the saphenous vein grafts (100%) than in the left anterior descending (LAD) (42%) or right coronary artery (39%).

Restenosis occurring within the stents has been treated with redilatation in 16 patients. At the present time 8 of those patients have been restudied and 6 have developed a second restenosis. Repeat dilatation within the stent produces an excellent angiographic appearance with very little elastic recoil due to the rigid stent wires in the media. Although the numbers are small at the present time, the restenosis observed after such a procedure, however, remains disquieting.

In a small subset of the patients, a vigorous antiproliferative program was attempted. In addition to the previously mentioned antithrombotic and antiplatelet agents, hydrocortisone and colchicine were administered to a group of patients.[15] Among these patients, 16 have undergone late restudy to evaluate symptoms or to perform a 6-month routine restudy. The restenosis rate in this group is not different from the overall group; however, there were 6 patients who developed aneurysms within the stented segment, an indication of nonhealing. This is the first documentation of altered healing in angioplasty, and although it is not a desired result, it is of some interest in the future investigation of restenosis strategies.

Since the results presented here, we have continued to utilize this stent and the Palmaz-Schatz stent as bailout devices in acute closure situations and have modified the poststent anticoagulation program slightly. Experience from other stent programs teaches us that the long-term results in larger arteries are significantly superior to those in smaller arteries. It is important to note that in this series, approximately 25% of the patients received 2.5-mm stents. Whereas late restenosis is an undesired outcome in the setting of acute closure with ischemic syndrome, the ability to bail out of that situation with a stent is quite desirable. The availability of stents for this purpose has become a major nonsurgical backup procedure for high-risk angioplasty. Virtually all patients undergoing angioplasty in our center are informed of the availability of stents and are asked to sign experimental protocols allowing the use of stents if necessary for the occurrence of a nonsolvable acute closure syndrome. However, because of the obvious added burden of prolonged anticoagulation and prolonged hospitalization, all efforts are aimed at solving the acute closure problems without stent placement.

STENTS USED FOR THE PREVENTION OF RESTENOSIS

The first large stent experience utilized for restenosis was with the self-expanding Wallstent in an investigation carried out entirely in Europe.[16] The first Wallstent was implanted in 1986. Between that time and March 1990, 265 patients were enrolled, with 308 lesions treated. One hundred seventy-three of those lesions were in native arteries and 135 in bypass grafts. Whereas the end point of the stent program was primarily to evaluate the effect on restenosis, some of the stents were placed for bailout purposes at the time of initial angioplasty. This occurred in 33% of the native stent implantations and in 4% of the vein graft implantations. Half of the native stent procedures were performed in restenotic lesions, and 21% of the bypass graft implantations were also for restenotic lesions. Anticoagulation was spottedly administered in the early portion of this experience, and there was a problem with thrombosis within 2 weeks of stent implantation in 15% of the patients. Of the patients who did not suffer early thrombotic closure, restenosis as defined by the 50% diameter definition occurred in 20% of the native coronary arteries and in 34% of the vein grafts. The restudy rate in this series was 82%, and it is important to emphasize that the studies were performed by automated edge detection quantitative angiographic measures in a core laboratory.

The conclusion that can be reasonably surmised from this data would suggest that whereas this particular stent, in the manner in which it was used, resulted in perhaps an unacceptable early thrombotic closure rate, the restenosis rate was respectable and perhaps reduced below what would have been expected for similar lesions not stented. This conclusion can only be speculative, of course, because a randomized trial has not been conducted.

The Palmaz-Schatz stent has undergone a carefully controlled trial to evaluate its effect on restenosis. An an-

giographic core laboratory has now been established to evaluate this stent.[17] Patients selected for this trial must have (1) objective evidence of ischemia, (2) critical stenoses greater than 70% by visual estimation, (3) preserved left ventricular function, and (4) suitability for coronary artery bypass surgery. Important exclusions were recent acute myocardial infarction, diffuse disease, ostial stenosis, large diseased side branches, pre-existent coronary thrombi, unprotected left main stenosis, and extreme vessel tortuosity. The protocol calls for aspirin therapy, 325 mg daily; dipyridamole, 75 mg three times a day; calcium channel antagonists; low-molecular-weight dextran; heparin, 1,000 units initially with continuous infusion or intermittent boluses to maintain activated clotting time greater than 300 seconds throughout the procedure; and following stent placement heparin administration continued for several days until warfarin therapy could increase the prothrombin time to greater than 16 seconds. Aspirin therapy is continued indefinitely, and dipyridamole and calcium antagonists are continued for 3 months. Coumadin anticoagulation is continued for 1 to 3 months. During the first phase of the trial of this stent, 226 patients underwent attempted placement, and 94%, or 213 patients, had successful stent placement. Subacute thrombosis, that is, thrombosis occurring within the first 2 weeks, occurred in 8 patients, or 3.8%. Excluding those patients, 205 patients were eligible for follow-up angiography, which was performed in 165 patients, or 80% of that group, 5.5 months following stent implantation. This study was limited to native coronary arteries; however, once again restenotic lesions were included and represent 65% of the total population.

Restenosis was determined by an automated edge detection computer-assisted quantitative methodology performed by a core angiographic laboratory. By utilizing the definition of a 50% stenosis at final follow-up, restenosis occurred in 34% of the patients. Subgroup analysis revealed some important differences. Placement of multiple stents resulted in a higher restenosis rate, with 21 of 40, or 53%, of the patients having restenosis. There was no difference in the restenosis rate relative to the artery stented. Previously observed higher restenosis rates with balloon angioplasty in the proximal anterior descending artery were not seen in this stent experience. Larger arteries had a better maintained patency, with arteries greater than 3.2 mm in diameter having a restenosis rate of 21% and arteries smaller than this having a restenosis rate of 37%. As mentioned, two thirds of these patients had restenotic lesions rather than de novo lesions. The restenosis rate for de novo lesions was 25% vs. 34% for restenotic lesions. In the subgroup that received a single stent for a de novo lesion, the restenosis rate was 13%. This study certainly achieved better early results, with perhaps more careful selection and vigorous anticoagulation playing a role. It is not clear whether the design of the stent, which as mentioned earlier differs significantly from the coil stents or the interdigitating mesh stents, is an important factor. There is clearly a broad range of restenosis rates depending on the type of lesion treated. This fact certainly calls for a randomized trial of stenting vs. balloon angioplasty in a wide array of lesions in which stenting shows promise. Such trials are currently in the planning stage.

FUTURE DIRECTIONS FOR CORONARY STENTING

Whereas coronary stenting seems to have proved to be an effective means of solving the abrupt closure of arteries, its effect on restenosis, although encouraging, needs significantly more study. The price of stenting remains high. The threat of thrombotic closure necessitates a vigorous anticoagulation program. The use of anticoagulants significantly increases the risk of bleeding complications, dramatically prolongs the patient's hospitalization, and increases costs. An effective anticoagulant and antiplatelet therapy that is administered systemically may reduce acute thrombotic closure but will not reduce the hemorrhagic complications unless some dramatic breakthroughs in antithrombotic therapy are achieved. Various agents including antithrombins and antiplatelet antibodies as well as polymers to inhibit platelet activity have been proposed and will soon undergo more extensive testing. Another approach is the application of such antithrombotic agents directly to stents, and many efforts are under way to incorporate these agents into the stent itself. This could be accomplished with the coating of existing metallic stents or the replacement of the metal stent with a totally polymer device. Such polymers could be biodegradeable or nondegradeable. In any case, the role for stenting in interventional cardiology will obviously be an important one for the future and, as with so many other breakthroughs, creates its own list of interesting problems for exploration by scientists in the future.

REFERENCES

1. Liu MW, Roubin GS, King SB III: Restenosis after coronary angioplasty: Potential biologic determinants and role of intimal hyperplasia. *Circulation* 1989; 79:1374–1387.
2. Chesebro JH, Lam JYT, Badimon L, et al: Restenosis after arterial angioplasty: A hemorrheologic response to injury. *Am J Cardiol* 1987; 60:10–16.
3. Dotter CT: Transluminally placed coil-spring endarterial

tube grafts, long-term patency in canine popliteal artery. *Invest Radiol* 1969; 4:329–332.

4. Schatz RA, Palmaz JC, Tio FO, et al: Balloon expandable intercoronary stents in the adult dog. *Circulation* 1987; 76:450–457.
5. Roubin GS, Robinson KA, King SB, et al: Early and late results of intracoronary arterial stenting after coronary angioplasty in dogs. *Circulation* 1987; 76:891–897.
6. Robinson KA, Roubin GS, Siegel RJ, et al: Intraarterial stenting in the atherosclerotic rabbit. *Circulation* 1988; 78:646–653.
7. Karas SP, Gravanis MB, Robinson KA, et al: Comparison of the response to coronary artery balloon injury and stenting in swine: An animal model of restenosis. *J Am Coll Cardiol*, in press.
8. Schwartz RS, Murphy JG, Edwards WD, et al: Restenosis after balloon angioplasty: Practical proliferative model in porcine coronary arteries. *Circulation* 1990; 82:2190–2200.
9. Detre KM, Holmes DR, Holubkov R, et al: Incidence and consequences of periprocedural occlusion. The 1985–1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. *Circulation* 1990; 82:739–750.
10. Talley JD, Weintraub WS, Roubin GS, et al: Failed elective percutaneous transluminal coronary angioplasty requiring coronary artery bypass surgery: In-hospital and late clinical outcome at 5 years. *Circulation* 1990; 82:1203–1213.
11. Serruys PW, Strauss BH, Beatt KJ, et al: Angiographic follow-up after placement of a self-expanding coronary artery stent. *N Engl J Med* 1991; 324:13–17.
12. deFeyter PJ, DeScheerder I, van den Brand M, et al: Emergency stenting for refractory acute coronary artery occlusion during coronary angioplasty. *Am J Cardiol* 1990; 66:1147–1150.
13. Roubin GS, Douglas JS Jr, Lembo NJ, et al: Intracoronary stenting for acute closure following percutaneous transluminal coronary angioplasty (PTCA). *Circulation* 1988; 78(suppl 2):407.
14. Roubin GS, King SB III, Douglas JS Jr, et al: Intracoronary stenting during percutaneous transluminal coronary angioplasty. *Circulation* 1990; 81(suppl 4):92–100.
15. Hearn JA, King SB III: Restenosis after Gianturco-Roubin stent placement for acute closure, in Serruys, PW, Strauss B, Kings S (eds): *Restenosis.* Dodrecht, The Netherlands, Kluwer, in press.
16. Rab ST, King SB, Roubin GS, et al: Coronary aneurysms following stent placement: A suggestion of altered vessel healing in the presence of anti-inflammatory agents. *J Am Coll Cardiol*, in press.
17. Bertrand ME, Puel J, Meier B, et al: The Wallstent experience: 1986–1990, in Serruys PW, Strauss B, King S, (eds): *Restenosis.* Dodrecht, The Netherlands, Kluwer, in press.
18. Schatz RA, Baim DS, Leon M, et al: Clinical experience with the Palmaz-Schatz coronary stent. Initial results of a multicenter study. *Circulation* 1991; 83:148–161.

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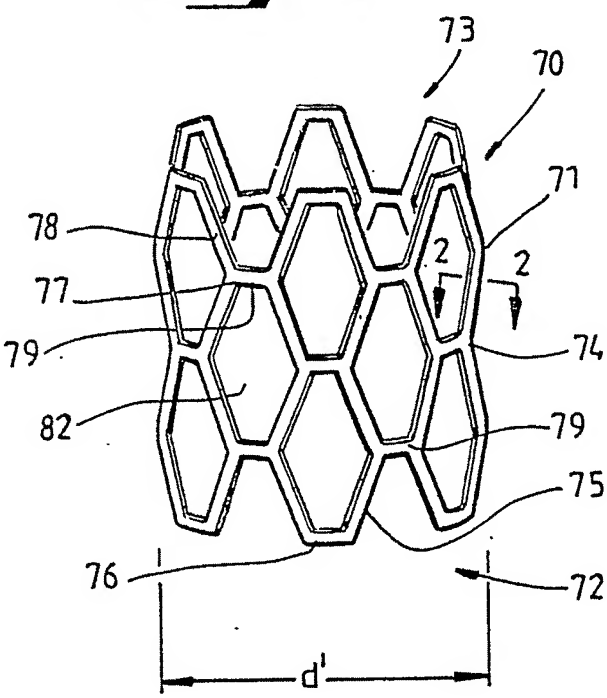
(54) **Expandable intraluminal graft.**

(57) A plurality of expandable and deformable intraluminal vascular grafts are expanded within a blood vessel by an angioplasty balloon associated with a catheter to dilate and expand the lumen of a blood vessel. The grafts may be thin-walled tubular members (71) having a plurality of slots (82) disposed substantially parallel to the longitudinal axis of the tubular members (71), and adjacent grafts are flexibly connected by a single connector member disposed substantially parallel to the longitudinal axis of the tubular members.

Fig. 1B



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EXPANDABLE INTRALUMINAL GRAFT

1. Field of the Invention.

The invention relates to an expandable intraluminal graft for use within a body passageway or duct and, more particularly, expandable intraluminal vascular grafts which are particularly useful for repairing blood vessels narrowed or occluded by disease; and a method and apparatus for implanting expandable intraluminal grafts.

2. Description of the Prior Art.

Intraluminal endovascular grafting has been demonstrated by experimentation to present a possible alternative to conventional vascular surgery. Intraluminal endovascular grafting involves the percutaneous insertion into a blood vessel of a tubular prosthetic graft and its delivery via a catheter to the desired location within the vascular system. Advantages of this method over conventional vascular surgery include obviating the need for surgically exposing, incising, removing, replacing, or bypassing the defective blood vessel.

Structures which have previously been used as intraluminal vascular grafts have included coiled stainless steel springs; helically wound coil springs manufactured from an expandable heat-sensitive material; and expanding stainless steel stents formed of stainless steel wire in a zig-zag pattern. In general, the foregoing structures have one major disadvantage in common. Insofar as these structures must be delivered to the desired location within a given body passageway in a collapsed state, in order to pass through the body passageway, there is no effective control over the final, expanded configuration of each structure. For example, the expansion of a particular coiled spring-type graft is predetermined by the spring constant and modulus of elasticity of the particular material utilized to manufacture the coiled spring structure. These same factors predetermine the amount of expansion of collapsed stents formed of stainless steel wire in a zig-zag pattern. In the case of intraluminal grafts, or prostheses, formed of a heat sensitive material which expands upon heating, the amount of expansion is likewise predetermined by the heat expansion characteristics of the particular alloy utilized in the manufacture of the intraluminal graft.

Thus, once the foregoing types of intraluminal grafts are expanded at the desired location within a body passageway, such as within an artery or vein, the expanded size of the graft cannot be changed. If the diameter of the desired body passageway has been miscalculated, an undersized graft might not expand enough to contact the interior surface of the body passageway, so as to be secured thereto. It may then migrate away from the desired location within the body passageway. Likewise, an oversized graft might expand to such an extent that the spring force, or expansion force, exerted by the graft upon the body passageway could cause rupturing of the body passageway. Further, the constant outwardly radiating force exerted upon the interior surface of the body passageway can cause erosion of the internal surface, or intima, of the artery or body passageway.

Another alternative to conventional vascular surgery has been percutaneous balloon dilation of elastic vascular stenoses, or blockages, through use of a catheter mounted angioplasty balloon. In this procedure, the angioplasty balloon is inflated within the stenosed vessel, or body passageway, in order to shear and disrupt the wall components of the vessel to obtain an enlarged lumen. With respect to arterial atheroscleerotic lesions, the relatively incompressible plaque remains unaltered, while the more elastic medial and adventitial layers of the body passageway stretch around the plaque. This process produces dissection, or a splitting and tearing, of the body passageway wall layers, wherein the intima, or internal surface of the artery or body passageway, suffers fissuring. This dissection forms a "flap" of underlying tissue which may reduce the blood flow through the lumen, or block the lumen. Typically, the distending intraluminal pressure within the body passageway can hold the disrupted layer or flap, in place. If the intimal flap created by the balloon dilation procedure is not maintained in place against the expanded intima, the intimal flap can fold down into the lumen and close off the lumen, or may even become detached and enter the body passageway. When the intimal flap closes off the body passageway, immediate surgery is necessary to correct this problem.

Although the balloon dilation procedure is typically conducted in the catheterization lab of a hospital, because of the foregoing problem, it is always necessary to have a surgeon on call should the intimal flap block the blood vessel or body passageway. Further, because of the possibility of the intimal flap tearing away from the blood vessel and blocking the lumen, balloon dilations cannot be performed upon certain critical body passageways, such as the left main coronary artery, which leads into the heart. If an intimal flap formed by a balloon dilation procedure abruptly comes down and closes off a critical body passageway, such as the left main coronary artery, the patient could die before

any surgical procedures could be performed.

Additional disadvantages associated with balloon dilation of elastic vascular stenoses is that many fail because of elastic recoil of the stenotic lesion. This usually occurs due to a high fibrocollagenous content in the lesion and is sometimes due to certain mechanical characteristics of the area to be dilated. Thus, although the body passageway may initially be successfully expanded by a balloon dilation procedure, subsequent, early restenosis can occur due to the recoil of the body passageway wall which decreases the size of the previously expanded lumen of the body passageway. For example, stenoses of the renal artery at the ostium are known to be refractory to balloon dilation because the dilating forces are applied to the aortic wall rather than to the renal artery itself. Vascular stenoses caused by neointimal fibrosis, such as those seen in dialysis-access fistulas, have proved to be difficult to dilate, requiring high dilating pressures and larger balloon diameters. Similar difficulties have been observed in angioplasties of graft-artery anastomotic strictures and postendarterectomy recurrent stenoses. Percutaneous angioplasty of Takayasu arteritis and neurofibromatosis arterial stenoses may show poor initial response and recurrence which is believed due to the fibrotic nature of these lesions.

For repairing blood vessels narrowed or occluded by disease, or repairing other body passageways, the length of the body passageway which requires repair, as by the insertion of a tubular prosthetic graft, may present problems if the length of the required graft cannot negotiate the curves or bends of the body passageway through which the graft is passed by the catheter. In other words, in many instances, it is necessary to support a length of tissue within a body passageway by a graft, wherein the length of the required graft exceeds the length of a graft which can be readily delivered via a catheter to the desired location within the vascular system. Some grafts do not have the requisite ability to bend so as to negotiate the curves and bends present within the vascular system, particularly prostheses or grafts which are relatively rigid and resist bending with respect to their longitudinal axes.

Accordingly, prior to the development of the present invention, there has been no expandable intraluminal vascular graft for expanding the lumen of a body passageway, which: prevents recurrence of stenoses in the body passageway; can be utilized for critical body passageways, such as the left main coronary artery of a patient's heart; prevents recoil of the body passageway wall; allows the intraluminal graft to be expanded to a variable size to prevent migration of the graft away from the desired location and prevents rupturing and/or erosion of the body passageway by the expanded graft; permits tissue of an elongated section of a body passageway to be supported by an elongated graft; and provides the necessary flexibility to negotiate the bends and curves in the vascular system. Therefore, the art has sought an expandable intraluminal vascular graft which: prevents recurrence of stenoses in the body passageway; is believed to be able to be utilized in critical body passageways, such as the left main coronary artery of the heart; prevents recoil of the body passageway; can be expanded to a variable size within the body passageway to prevent migration of the graft away from the desired location and to prevent rupturing and/or erosion of the body passageway by the expanded graft; permits tissue of an elongated section of a body passageway to be supported by an elongated graft; and provides the necessary flexibility to negotiate the bends and curves in the vascular system.

SUMMARY OF THE INVENTION

In accordance with the invention, the foregoing advantages have been achieved by the present expandable intraluminal vascular graft. The present invention includes a plurality of thin-walled tubular members, each having first and second ends and a wall surface disposed between the first and second ends, the wall surface having a substantially uniform thickness and a plurality of slots formed therein, the slots being disposed substantially parallel to the longitudinal axis of each tubular member; a single connector member being disposed between adjacent tubular members to flexibly connect adjacent tubular members, the single connector member being disposed in a substantially parallel relationship with respect to the longitudinal axis of the tubular members and coplanar with each tubular member; each tubular member having a first diameter which permits intraluminal delivery of the tubular members into a body passageway having a lumen; and the tubular members having a second, expanded and deformed diameter, upon the application from the interior of the tubular members of a radially, outwardly extending force, which second diameter is variable and dependent upon the amount of force applied to the tubular members, whereby the tubular members may be expanded and deformed to expand the lumen of the body passageway.

A further feature of the present invention is that the single connector member may be a thin-walled, elongate bar member, coplanar with adjacent tubular members. An additional feature of the present invention is that a first connector member may be disposed between the second end of a first tubular

member and the first end of a second tubular member; a second connector member may be disposed between the second end of the second tubular member and the first end of a third tubular member; the first and second connector members being angularly offset from one another with respect to the longitudinal axis of the tubular members.

The expandable intraluminal vascular graft of the present invention, when compared with previously proposed prior art intraluminal grafts, has the advantages of: preventing recurrence of stenoses; is believed to permit implantation of grafts in critical body passageways, such as in the left main coronary artery of the heart; prevents recoil of the body passageway; prevents erosion of the body passageway by the expanded graft; permits expansion of the graft to a variable size dependent upon conditions within the body passageway; permits tissue of an elongated section of a body passageway to be supported by an elongated graft; and provides the necessary flexibility to negotiate the bends and curves in tortuous body passageways, such as the vascular system.

BRIEF DESCRIPTION OF THE DRAWINGS:

In the drawings:

FIG. 1A is a perspective view of an expandable intraluminal vascular graft, or prosthesis for a body passageway, having a first diameter which permits delivery of the graft, or prosthesis, into a body passageway;

FIG. 1B is a perspective view of the graft, or prosthesis, of FIG. 1A, in its expanded configuration when disposed within a body passageway;

FIG. 2 is a cross-sectional view of the prosthesis taken along line 2-2 of FIG. 1B;

FIG. 3 is a cross-sectional view of an apparatus for intraluminally reinforcing a body passageway, or for expanding the lumen of a body passageway, illustrating a prosthesis, or intraluminal vascular graft, in the configuration shown in FIG. 1A;

FIG. 4 is a cross-sectional view of the apparatus for intraluminally reinforcing a body passageway, or for expanding the lumen of a body passageway, with the graft, or prosthesis, in the configurations shown in FIG. 1B;

FIGS. 5 and 6 are perspective views of prostheses for a body passageway, with the grafts, or prostheses, having a coating thereon;

FIG. 7 is a perspective view of another embodiment of a graft or prosthesis in accordance with the present invention; and

FIG. 8 is a perspective view of the graft of FIG. 7, wherein the graft has been bent or articulated.

While the invention will be described in connection with the preferred embodiment, it will be understood that it is not intended to limit the invention to that embodiment. On the contrary, it is intended to cover all alternatives, modifications, and equivalents, as may be included within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION:

In FIGS. 1A and 1B, an expandable intraluminal vascular graft, or expandable prosthesis for a body passageway, 70 is illustrated. It should be understood that the terms "expandable intraluminal vascular graft" and "expandable prosthesis" are interchangeably used to some extent in describing the present invention, insofar as the methods, apparatus, and structures of the present invention may be utilized not only in connection with an expandable intraluminal vascular graft for expanding partially occluded segments of a blood vessel, or body passageway, but may also be utilized for many other purposes as an expandable prosthesis for many other types of body passageways. For example, expandable prostheses 70 may also be used for such purposes as: (1) supportive graft placement within blocked arteries opened by transluminal recanalization, but which are likely to collapse in the absence of an internal support; (2) similar use following catheter passage through mediastinal and other veins occluded by inoperable cancers; (3) reinforcement of catheter created intrahepatic communications between portal and hepatic veins in patients suffering from portal hypertension; (4) supportive graft placement of narrowing of the esophagus, the intestine, the ureters, the urethra; and (5) supportive graft reinforcement of reopened and previously obstructed bile ducts. Accordingly, use of the term "prosthesis" encompasses the foregoing usages within various types of body passageways, and the use of the term "intraluminal vascular graft" encompasses use for expanding the lumen of a body passageway. Further, in this regard, the term "body passageway" encompasses any duct within the human body, such as those previously described, as well as any vein, artery, or blood vessel within the human vascular system.

Still with reference to FIGS. 1A and 1B, the expandable intraluminal vascular graft, or prosthesis, 70 is shown to generally comprise a tubular member 71 having first and second ends 72, 73 and a wall surface 74 disposed between the first and second ends 72, 73. Tubular member 71 has a first diameter, d, which, to be hereinafter described

in greater detail, permits intraluminal delivery of the tubular member 71 into a body passageway 80 having a lumen 81 (FIG. 3). With reference to FIG. 1B, upon the application from the interior of the tubular member 71 of a radially, outwardly extending force, to be hereinafter described in greater detail tubular member 71 has a second, expanded diameter, d', which second diameter d' is variable in size and dependent upon the amount of force applied to deform the tubular member 71.

Tubular member 71, may be any suitable material which is compatible with the human body and the bodily fluids (not shown) with which the vascular graft, or prosthesis, 70 may come into contact. Tubular member 71 must also be made of a material which has the requisite strength and elasticity characteristics to permit the tubular member 71 to be expanded and deformed from the configuration shown in FIG. 1A to the configuration shown illustrated in FIG. 1B and further to permit the tubular member 71 to retain its expanded and deformed configuration with the enlarged diameter d' shown in FIG. 1B and resist radial collapse. Suitable materials for the fabrication of tubular member 71 would include silver, tantalum, stainless steel, gold, titanium or any suitable plastic material having the requisite characteristics previously described.

Preferably, tubular member 71 is initially a thin-walled stainless steel tube having a uniform wall thickness, and a plurality of slots 82 are formed in the wall surface 74 of tubular member 71. As seen in FIG. 1A when tubular member 71 has the first diameter d, the slots 82 are disposed substantially parallel to the longitudinal axis of the tubular member 71. As seen in FIG. 1A, the slots 82 are preferably uniformly and circumferentially spaced from adjacent slots 82, as by connecting members 77, which connecting members 77 preferably have a length equal to the width of slots 82, as seen in FIG. 1A. Slots 82 are further uniformly spaced from adjacent slots 82 along the longitudinal axis of the tubular member 71, which spacing is preferably equal to the width of connecting members 77. Thus, the formation of slots 82 results in at least one elongate member 75 being formed between adjacent slots 82, elongate member 75 extending between the first and second ends, 72, 73 of tubular member 71, as seen in FIG. 1A.

Still with reference to FIG. 1A, each slot will have first and second ends with a connecting member 77 disposed at the first and second ends of slots 82. Preferably, the first and second ends of each slot 82 are disposed intermediate the first and second ends of adjacent slots 82 along the longitudinal axis of the tubular member 71. Thus, connecting members 77, which are disposed at the first and second ends of each slot 82, and between elongate members 75, will in turn be disposed intermediate the first and second ends of adjacent slots 82 along the longitudinal axis of the tubular member 71. Accordingly, slots 82 are preferably uniformly and circumferentially spaced from adjacent slots, and slots 82 adjacent to one another along the longitudinal axis of tubular member 71 are in a staggered relationship with one another. Alternating slots disposed about the circumference of tubular member 71 at both the first and second ends 72, 73 of tubular member 71 will only have a length equal to approximately one-half of the length of a complete slot 82, such half-slot 82 being bounded by members 78, 79, at both the first and second ends 72, 73 of tubular member 71. Although the graft, or prosthesis, 70 of FIGS. 1A and 1B is illustrated to have a length approximately equal to the length of two slots 82, it should be apparent that the length of the graft 70 could be made longer or shorter as desired.

The foregoing described construction of graft, or prosthesis, 70 permits graft, or prosthesis, 70 to be expanded uniformly, and outwardly, in a controlled manner into the configuration shown in FIG. 1B, upon the application of a suitable force from the interior of tubular member 71, as will be hereinafter described in greater detail. The expansion of tubular member 71 into the configuration shown in FIG. 1B is further uniform along the length of tubular member 71, not only because of the uniform spacing between slots 82, as previously described, but also because the thickness of the wall surface 74, or the thickness of connecting members 77, elongate members 75, and members 78, 79, is the same uniform thickness. As illustrated in FIG. 2, the uniform thickness of elongate member 75 is shown, and the preferred cross-sectional configuration of elongate member 75, connecting member 77, and members 78, 79, is illustrated, which configuration is rectangular. It should of course be understood by those skilled in the art, that the cross-sectional configuration of the foregoing components of graft, or prosthesis, 70 could also be square, rectangular, or other cross-sectional configurations. As will be hereinafter described in greater detail, it is preferable that the outer surface 74 of graft, or prothesis, 70, which would be in contact with the body passageway 80 FIG. 4, should be relatively smooth.

With reference to FIG. 1B, it is seen that after the graft, or prosthesis 70, has been expanded and deformed into the configuration of FIG. 1B, the slots 82 will assume a substantially hexagonal configuration when the tubular member 71 has the second, expanded diameter, d', as shown in FIG. 1B. Such a hexagonal configuration will result when the slots 82 initially have a substantially rectangular configuration when the tubular member 71 has the first diameter, d, illustrated in FIG. 1A. It should be

noted that were the width of slots 82 to be substantially reduced, whereby the length of connecting member 77 would approximate a single point intersection, the expansion of such a tubular member 71 would result in slots 82 assuming a configuration which would be substantially a parallelogram (not shown).

It should be noted that not only is tubular member 71 expanded from the configuration shown in FIG. 1A to achieve the configuration shown in FIG. 1B, but tubular member 71 is further "deformed" to achieve that configuration. By use of the term "deformed" is meant that the material from which graft, or prosthesis, 70 is manufactured is subjected to a force which is greater than the elastic limit of the material utilized to make tubular member 71. Accordingly, the force is sufficient to permanently bend elongate members 75 whereby segments of the elongate members 75 pivot about connecting members 77 and move in a circumferential direction as they pivot, whereby the diameter of the tubular member 71 increases from the first diameter, d, to the expanded diameter, d′, of FIG. 1B. The force to be applied to expand tubular member 71, which is applied in the manner which will be hereinafter described in greater detail, must thus be sufficient to not only expand tubular member 71, but also to deform elongate member 75, in the manner previously described, whereby the portions of the elongate members 75 which pivot about the ends of connecting members 77 do not "spring back" and assume their configuration shown in FIG. 1A, but rather retain the configuration thereof in FIG. 1B. Once graft, or prosthesis, 70 has been expanded and deformed into the configuration shown in FIG. 1B, graft, or prosthesis 70, will serve to prevent a body passageway from collapsing as will be hereinafter described in greater detail. It should be noted that when tubular member 71 has the first diameter, d, shown in FIG. 1A, or after tubular member 71 has been expanded and deformed into the second, expanded diameter, d′, of FIG. 1B, tubular member 71 does not exert any outward, radial force, in that tubular member 71 is not a "spring-like" or "self-expanding member", which would tend to exert an outwardly radial force.

With reference now to FIGS. 3 and 4, apparatus of the present invention will be described in greater detail. Once again, it should be understood that the apparatus of the present invention is useful not only for expanding the lumen of a body passageway, such as an artery, vein, or blood vessel of the human vascular system, but are also useful to perform the previously described procedures to intraluminally reinforce other body passageways or ducts, as previously described. Still with reference to FIGS. 3 and 4, an expandable intraluminal vascular graft, or prosthesis, 70, of the type described in connection with FIGS. 1A and 1B, is disposed or mounted upon a catheter 83. Catheter 83 has an expandable, inflatable portion 84 associated therewith. Catheter 83 may include means for mounting and retaining 85 the expandable intraluminal vascular graft, of prosthesis, 70 on the expandable, inflatable portion 84 of catheter 83. The mounting and retaining means 85 could comprise retainer ring members 86 disposed on the catheter 83 adjacent the expandable inflatable portion 84 of catheter 83; and a retainer ring member 86 is disposed adjacent each end 72, 73 of the expandable intraluminal vascular graft, or prosthesis, 70. As seen in FIG. 3, retainer ring members could be formed integral with catheter 83, and the retainer ring member 86 adjacent the leading tip 87 of catheter 83 slopes upwardly and away from catheter tip 87 in order to protect and retain graft or prosthesis, 70 as it is inserted into the lumen 81 of body passageway 80, as to be hereinafter described in greater detail. The remaining retainer ring member 86 as shown in FIG. 3, slopes downwardly away from tip 87 of catheter 83, to insure easy removal of catheter 83 from body passageway 80. After expandable intraluminal graft, or prosthesis, 70 has been disposed upon catheter 83, in the manner previously described, the graft, or prosthesis, 70 and catheter 83 are inserted within a body passageway 80 by catheterization of the body passageway 80 in a conventional manner.

In a conventional manner, the catheter 83 and graft, or prosthesis, 70 are delivered to the desired location within the body passageway 80, whereat it is desired to expand the lumen 81 of body passageway 80 via intraluminal graft 70, or where it is desired to implant prosthesis 70. Fluoroscopy, and/or other conventional techniques may be utilized to insure that the catheter 83 and graft, or prosthesis, 70 are delivered to the desired location within the body passageway. Prosthesis, or graft, 70 is then controllably expanded and deformed by controllably expanding the expandable, inflatable portion 84 of catheter 83, whereby the prosthesis, or graft, 70 is expanded and deformed radially, outwardly into contact with the body passageway 80, as shown in FIG. 4. In this regard, the expandable, inflatable portion of catheter 83 may be a conventional angioplasty balloon 88. After the desired expansion and deformation of prosthesis, or graft, 70 has been accomplished, angioplasty balloon 88 may be collapsed, or deflated, and the catheter 83 may be removed in a conventional manner from body passageway 80. If desired, as seen in FIG. 3, catheter 83, having graft or prosthesis, 70 disposed thereon, may be initially encased in a conventional Teflon sheath 89, or a sheath 89 made of another suitable material, which

is pulled away from prosthesis, or graft, 70, prior to expansion of the prosthesis, or graft, 70.

Still with reference to FIGS. 3 and 4, it should be noted that tubular member 71 of prosthesis, or graft, 70 initially has the first predetermined, collapsed diameter, d, as described in connection with FIG. 1A, in order to permit the insertion of the tubular member, 71 into the body passageway 80 as previously described. When it is desired to implant prosthesis 70 within a body passageway 80 for the purposes previously described, the prosthesis 70 is, controllably expanded and deformed to the second diameter, d', and the second, expanded diameter, d', is variable and determined by the internal diameter of the body passageway 80, as shown in FIG. 4, and by the amount of expansion of the inflatable portion 84 of catheter 83. Accordingly, the expanded and deformed prosthesis 70, upon deflation of angioplasty balloon 88 will not be able to migrate from the desired location within the body passageway 80, nor will the expansion of the prosthesis 70 be likely to cause a rupture of the body passageway 80. Furthermore, insofar as prosthesis, or graft, 70 is not a "spring-like" or "self-expanding member", the prosthesis is not consistently applying an outward, radial force against the interior surface of body passageway 80, in excess of that required to resist radial collapse of the body passageway 80. Thus, erosion of the interior surface, or intima, of the artery or body passageway is prevented.

When it is desired to use expandable intraluminal graft 70 to expand the lumen 81 of a body passageway 80 having an area of stenosis, the expansion of intra luminal vascular graft 70 by angioplasty balloon 88, allows controlled dilation of the stenotic area and, at the same time controlled expansion and deformation of the vascular graft 70, whereby vascular graft 70 prevents the body passageway 80 from collapsing and decreasing the size of the previously expanded lumen 81. Once again, the second, expanded diameter d' of intraluminal vascular graft 70, as shown in FIG. 4, is variable and determined by the desired expanded internal diameter of body passageway 80. Thus, the expandable intraluminal graft 70 will not migrate away from the desired location within the body passageway 80 upon deflation of angioplasty balloon 88, nor will the expansion of intraluminal graft 70 likely cause a rupture of body passageway 80, nor any erosion as previously described. Further, should an intimal flap, or fissure, be formed in body passageway 80 at the location of graft 70, graft 70 will insure that such an intimal flap will not be able to fold inwardly into body passageway 80, nor tear loose and flow through body passageway 80. In the situation of utilizing graft 70 in the manner previously described to expand the lumen of a portion of a critical body passageway, such as the left main coronary artery, it is believed that the intimal flap will be unable to occlude the left main coronary artery of the heart and cause the death of the patient.

Because it is only necessary to inflate angioplasty balloon 88 one time in order to expand and deform graft 70, it is believed that a greater amount of endothelium, or inner layer of the intima, or inner surface of the body passageway, will be preserved, insofar as the extent of endothelial denudation during transluminal angioplasty is proportional to the balloon inflation time. Further, in theory, the amount of preserved endothelium should be large because in the expanded configuration of graft 70, potentially 80% of the endothelium is exposed through the openings or expanded slots 82 of graft 70. It is further believed that intact patches of endothelium within expanded slots 82 of graft 70 may result in a rapid, multicentric endothelialization pattern as shown by experimental studies.

With reference now to FIGS. 5 and 6, prostheses, or grafts, 70 of the type previously described in connection with FIGS. 1A and 1B are shown, and the tubular members 71 of grafts, or prostheses, 70 have a biologically inert or biologically compatible coating 90 placed upon wall surfaces 74 of tubular shaped members 71. Examples of a suitable biologically inert coating would be porous polyurethane, Teflon™, or other conventional biologically inert plastic materials. The coating 90 should be thin and highly elastic so as not to interfere with the desired expansion and deformation of prosthesis, or graft, 70. Coating 90 may be further provided with a means for anchoring 91 (FIG. 6) the tubular member 71 to the body passageway 80. Anchoring means 91 may be comprised of a plurality of radially, outwardly extending projections 92 formed on the coating 90. As seen in FIG. 6, the radially outwardly extending projections 92 could comprise a plurality of ridges 93, or other types of radially, outwardly extending projections. Further, it may be desirable to have a plurality of openings 94 formed in coating 90, as shown in FIG. 5, whereby the fluid contained in body passageway 80 can be in direct contact with the dilated, or expanded, body passageway area. Examples of biologically compatible coatings 90 would include coatings made of absorbable polymers such as those used to manufacture absorbable sutures. Such absorbable polymers include polyglycoides, polylactides, and copolymers thereof. Such absorbable polymers could also contain various types of drugs, whereby as the coating 90 is absorbed, or dissolves, the drug would be slowly released into the body passageway 80.

Turning now to FIGS. 7 and 8, an expandable

intraluminal vascular graft, or prosthesis, 70′ is shown for implantation in curved body passageways 80, or for use in the elongated sections of body passageway 80, when a prosthesis or a graft, 70′ is required which is longer than the graft, or prosthesis, 70 of FIG. 1A. Identical reference numerals are used throughout FIGS. 7 and 8 for elements which are the same in design, construction, and operation, as those previously described in connection with FIGS. 1A-6, and primed reference numerals are used for elements which are similar in construction, design, and operation, as those previously described in connection with 1A-6.

As seen in FIG. 7, graft, or prosthesis, 70′ generally includes a plurality of prostheses, or grafts, 70 as described previously in connection with FIGS. 1A, 1B, and 2. Disposed between adjacent tubular members, 71, or adjacent grafts, or prostheses, 70, is a single connector member 100 to flexibly connect adjacent tubular members 71 or grafts, or prostheses, 70. Connector members 100 are preferably formed of the same material as grafts 70, as previously described, and connector members 100 may be formed integrally between adjacent grafts 70, or tubular members 71, as shown in FIG. 7. The cross-sectional configuration of connector members 100, along the longitudinal axis of graft, or prosthesis, 70′, is the same, in that connector members 100 have the same uniform wall thickness of elongate members 75 and thus form a thin-walled, elongate bar member 101 which is coplanar with adjacent tubular members 71. Of course, it should be readily apparent to one of ordinary skill in the art, that the thickness of connector members 100 could alternatively be smaller than elongate member 75; however, it is preferable that the outer circumferential surface 102 of connector members 100 lies in the same plane formed by the wall surfaces 74 of grafts, or prostheses, 70, as seen in FIG. 7.

Still with reference to FIGS. 7-8, it should be noted that although graft, or prosthesis, 70′ is illustrated as including three grafts, or prostheses, 70 flexibly connected to one another by connector members 100, as few as two grafts 70 could be connected to form graft, or prosthesis, 70′. Furthermore, many grafts 70 could be flexibly connected by connector members 100 as are desired to form graft, or prosthesis, 70′. Preferably, the length of each graft, or prosthesis, 70 is approximately the length of two slots 82; however, the length of each graft 70 could be approximately equal to the length of two or more slots 82. When three or more grafts 70 are flexibly connected by connector members 100, as shown in FIGS. 7 and 8, preferably a first connector member 100 is disposed between the second end 73 of a first tubular member 70A and the first end 72 of a second tubular member 70B. A second connector member 100 is then disposed between the second end 73 of the second tubular member 70B and the first end 72 of a third tubular member 70C. The first and second connector members 100, as shown in FIGS. 7 and 8, may be angularly offset from one another with respect to the longitudinal axis of the tubular members 70 to permit the requisite flexibility between the interconnected grafts, or prostheses, 70.

The delivery and expansion of graft, or prosthesis, 70′ is the same as that previously described in connection with FIGS. 1A, 1B, and 3-4. The length of the expandable, inflatable portion 84 of catheter 83 would be sized to conform with the length of the graft, or prosthesis, 70′, as should be readily apparent to one of ordinary skill in the art. Except for the length of the expandable, inflatable portion 84, catheter 83, the method of delivery of graft, or prosthesis, 70′ and its subsequent, controllable expansion and deformation are the same as previously described. As seen in FIG. 8, the prosthesis 70′ is illustrated in the configuration it would assume when being delivered to the desired location within the body passageway 80, and the graft, or prosthesis, 70′ is disposed upon catheter 83 and is passing through a curved portion of body passageway 80, such as an arterial bend. Because of the disposition of flexible connector members 100 between adjacent tubular members 71, or grafts, or prostheses, 70, graft, or prosthesis, 70′ is able to flexibly bend, or articulate, with respect to the longitudinal axis of graft, or prosthesis, 70′, so as to be able to negotiate the curves or bends found in body passageways 80. It should be noted that connector members 100 permit the bending, or articulation of adjacent tubular members 71 in any direction about the longitudinal axis of graft, or prosthesis, 70′. When graft, or prosthesis, 70′ is in its expanded, and deformed configuration, tubular members 71 of graft, or prosthesis, 70′, will assume the configuration shown in FIG. 1B.

It is to be understood that the invention is not to be limited to the exact details of construction, operation, exact materials, or embodiments shown and described, as obvious modifications and equivalents will be apparent to one skilled in the art. Accordingly, the invention is therefore to be limited only by the scope of the appended claims.

Claims

1. An expandable intraluminal vascular graft, comprising:
a plurality of thin-walled tubular members, each having first and second ends and a wall surface disposed between the first and second ends, the wall surface having a substantially uniform thick-

ness and a plurality of slots formed therein, the slots being disposed substantially parallel to the longitudinal axis of each tubular member;

a single connector member being disposed between adjacent tubular members to flexibly connect adjacent tubular members, the single connector member being disposed in a substantially parallel relationship with respect to the longitudinal axis of the tubular members and coplanar with each tubular member.

each tubular member having a first diameter which permits intraluminal delivery of the tubular members into a body passageway having a lumen; and

the tubular members having a second, expanded and deformed diameter, upon the application from the interior of the tubular members of a radially, outwardly extending force, which second diameter is variable and dependent upon the amount of force applied to the tubular members, whereby the tubular members may be expanded and deformed to expand the lumen of the body passageway.

2. The expandable intraluminal graft of claim 1, wherein the single connector member is a thin-walled, elongate bar member, coplanar with adjacent tubular members.

3. The expandable intraluminal graft of claim 1, wherein a first connector member is disposed between the second end of a first tubular member and the first end of a second tubular member; a second connector member is disposed between the second end of the second tubular member and the first end of a third tubular member, the first and second connector members being angularly offset from one another with respect to the longitudinal axis of the tubular members.

4. An expandable prosthesis for a body passageway, comprising:

a plurality of thin-walled tubular members, each having first and second ends and a wall surface disposed between the first and second ends, the wall surface having a substantially uniform thickness and a plurality of slots formed therein, the slots being disposed substantially parallel to the longitudinal axis of each tubular member;

a single connector member being disposed between adjacent tubular members to flexibly connect adjacent tubular members, the single connector member being disposed in a substantially parallel relationship with respect to the longitudinal axis of the tubular members and coplanar with each tubular member;

each tubular member having a first diameter which permits intraluminal delivery of the tubular members into a body passageway having a lumen; and

the tubular members having a second, expanded and deformed diameter, upon the application from the interior of the tubular members, of a radially, outwardly extending force, which second diameter is variable and dependent upon the amount of force applied to the tubular member, whereby the tubular member may be expanded and deformed to expand the lumen of the body passageway.

5. The expandable prosthesis of claim 4, wherein the single connector member is a thin-walled, elongate bar member, coplanar with adjacent tubular members.

6. The expandable prosthesis of claim 4, wherein a first connector member is disposed between the second end of a first tubular member and the first end of a second tubular member; a second connector member is disposed between the second end of the second tubular member and the first end of a third tubular member, the first and second connector members being angularly offset from one another with respect to the longitudinal axis of the tubular members.

Fig.1A

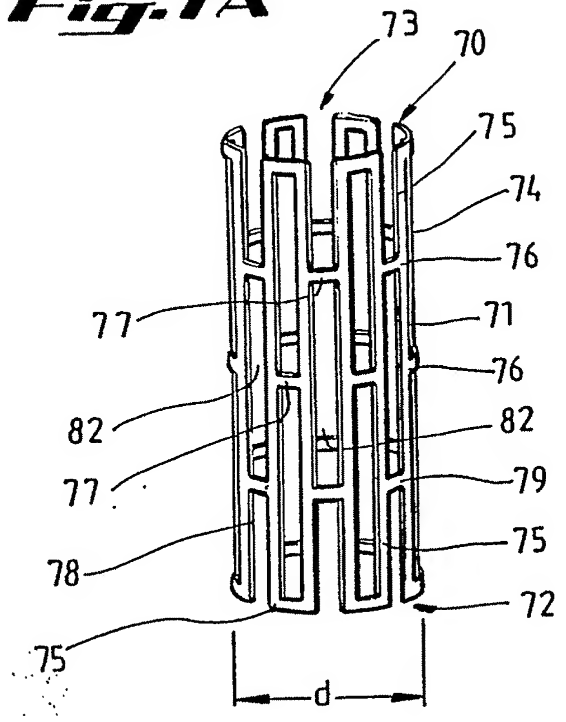


Fig.1B

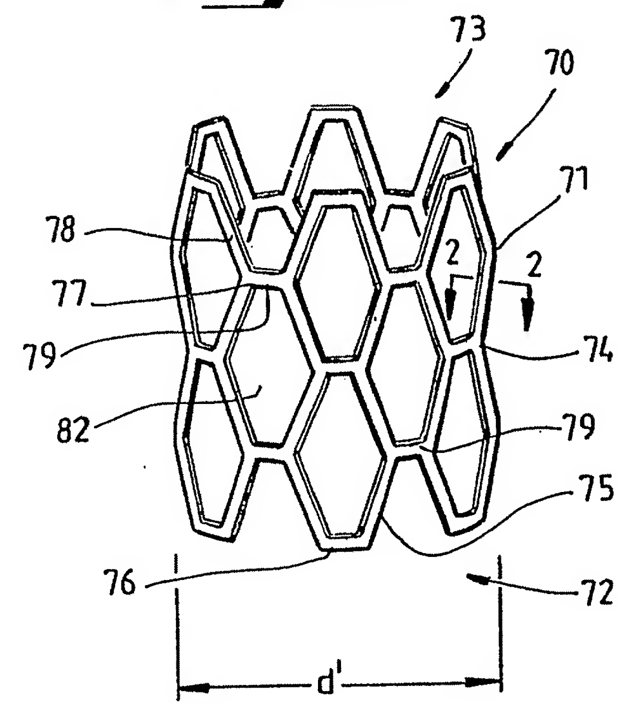


Fig.2

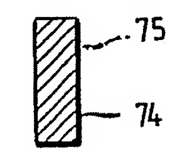
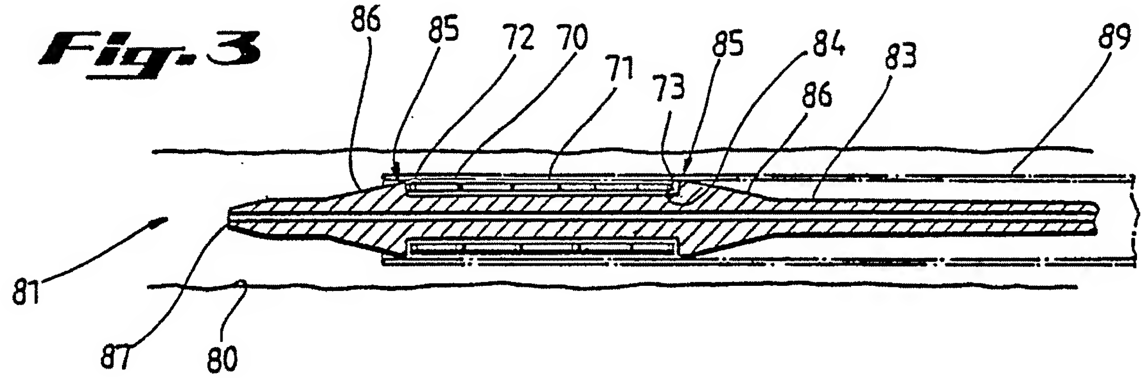


Fig. 3



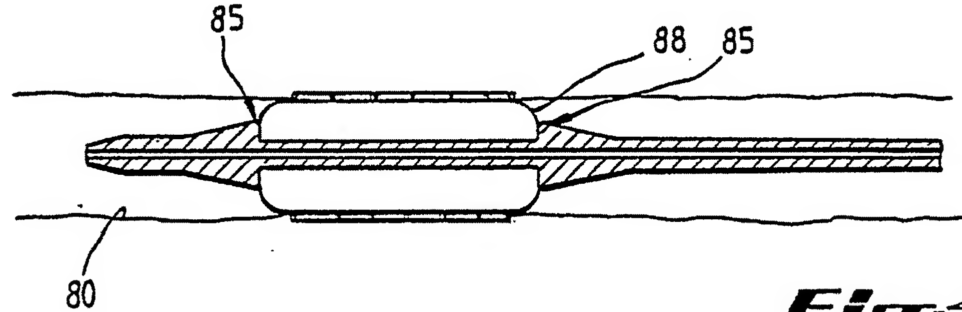
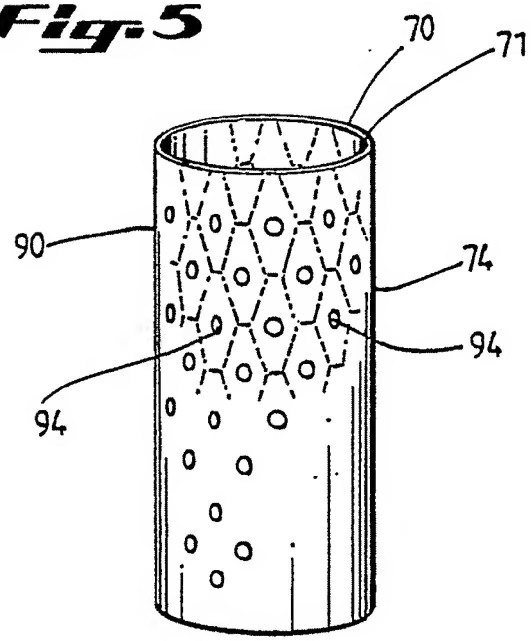


Fig. 4

Fig. 5



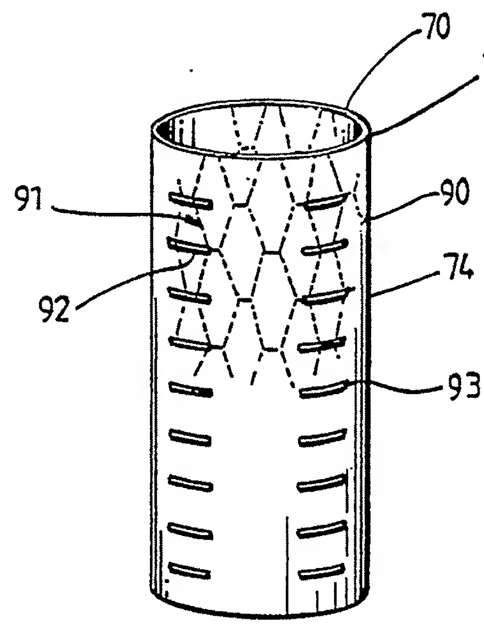


Fig. 6

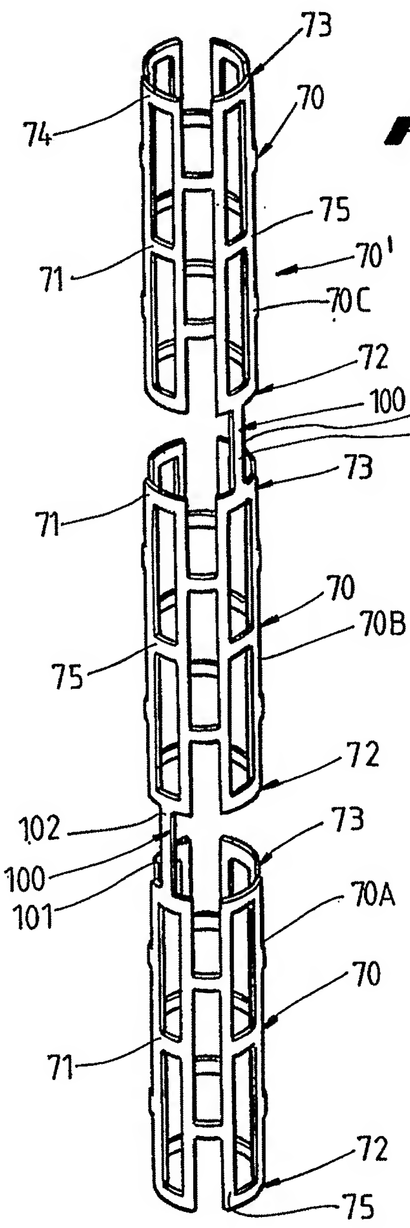

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Fig-7

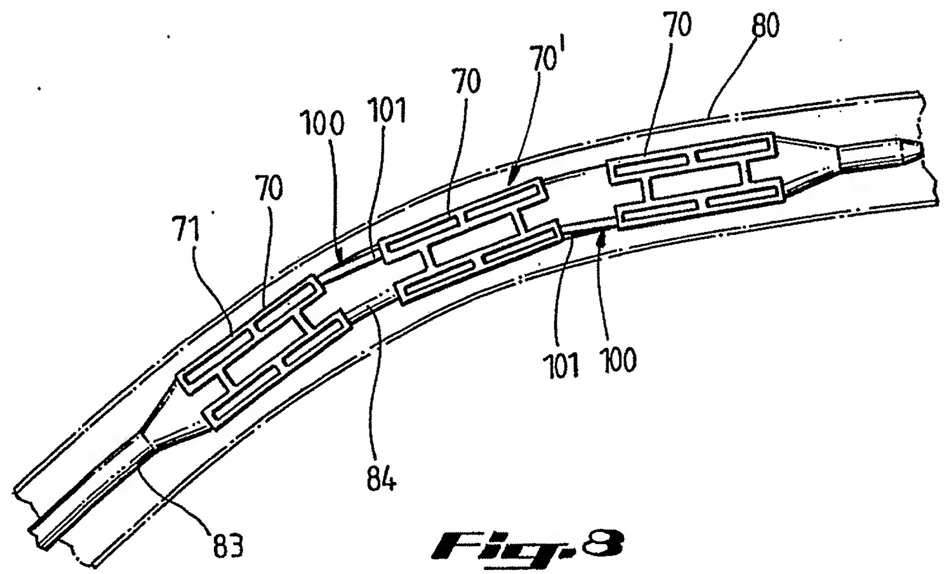
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Fig-8

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 89 11 8069

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
A	US-A-3 657 744 (ERSEN) * Abstract; column 3, lines 41-55; figures 3,4 * ---	1,3,4	A 61 F 2/06
A	EP-A-0 177 330 (COOK INC.) ---		
A	EP-A-0 282 175 (COOK INC.) ---		
A	EP-A-0 221 570 (PALMAZ) ---		
E	EP-A-0 335 341 (PALMAZ) * Abstract; figures * -----	1,2,4,5	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 F

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	10-01-1990	STEENBAKKER J.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EUROPEAN PATENT OFFICE,
Erhardtstrasse 27,
D-80331 MUNICH,
GERMANY

DECLARATION OF JEROME SEGAL, M.D.

I, Jerome Segal declare as follows:

1. I am an interventional cardiologist and have been since 1987. I am board certified in internal medicine, cardiovascular disease, and interventional cardiology. Since 2002, I have been an attending physician at Stanford University, where I perform coronary interventions at the Palo Alto Veterans Administration (VA) Hospital on average between one and two days per week. From 1988 through 2002, I was a professor of medicine at George Washington University in Washington DC. For seven of those years (from 1990-1997), I was Director of the Cardiac Catheterization Laboratories, where all coronary angioplasty and stenting procedures were performed. A copy of my *curriculum vitae* is attached as Exhibit 1.

2. I have been implanting coronary stents in humans since approximately 1990. At that time, I was a Principal Investigator for the Gianturco-Roubin stent, which was undergoing clinical trials in the U.S. Since then, I estimate that I have implanted approximately 1,600 coronary stents in humans. In the last 15 years I have implanted stents of varying designs from each of the different major manufacturers. This includes, for example, the Multi-Link family of stents from Guidant Corp., the NIR and Taxus from Boston Scientific, Inc., the GFX, BeStent and S-type family of stents from Medtronic, Inc., and the array of stents made by Johnson & Johnson, Inc./Cordis, such as the early Palmaz-Schatz-type stents.

3. For over 15 years I also have been heavily involved in the design and development of cardiovascular medical devices. I hold approximately 15 patents directed to such products, and several more are pending. In addition to my role as an attending physician at Stanford University, I am also currently President and CEO of Ouroboros, Inc. in San Diego, CA. Ouroboros, Inc. is a medical device company focused on the development of implants for spinal disease. Prior to Ouroboros, Inc., I was President and CEO of Medluminal Systems, Inc. (formerly Radiovascular Systems, Inc.) in Palo Alto, California. Medluminal Systems develops novel catheters for use in angioplasty procedures. Prior to that I was President and CEO of Cardiometrics, Inc. Cardiometrics was involved in the development and marketing of catheter based devices used in interventional cardiology.

4. I received my medical degree from the Tufts University School of Medicine in 1980, after which I completed my internship and residency in internal medicine at Harvard University (Beth Israel Hospital) in 1983. After completing my residency, I completed a three year cardiology fellowship at Stanford University and then completed a postdoctoral fellowship in coronary interventions at Sequoia Hospital, in Redwood City, California in 1987.

5. I have been asked to review published patent application WO-A-97 33532 to Medtronic, Inc., which I understand is referred to as D1 here. I focused primarily on the stent shown in Figure 7A and its corresponding disclosure within the text of D1.

6. In my opinion, a person of skill in the art could easily imagine the way in which the expandable stent shown in Figure 7A of D1 would change in shape upon compression. Upon review of D1, I agree with the European Patent Office (EPO) Panel that if the stent shown in Figure 7A was compressed from its shown state, the various parts of the stent would shrink in radial and longitudinal directions. The ultimate result is that the ring frames will get smaller in diameter and the flexure means would still be curved.

7. I also have been asked to review PCT publication PCT/US95/08975, entitled "A Flexible Expandable Stent," referred to in these proceedings as D2.

8. The stent design shown in Figures 1 through 4 of D2 has sharp corners that cause stress concentration, as would be recognized by one of skill in the art. The concept of stress

concentrations at corners and other changes in cross-section is well-known to one skilled in the art of stent design, and for that matter, medical device design. Stent design must account for the distribution of stress due to the ongoing loads to which the devices are subject, i.e., the flow of pumping blood, contraction of the heart and movement of the vessels. And ultimately, it should be remembered that such a device must be capable of implantation for extended periods of time.

9. In addition, from a practical standpoint, a person of skill in the art seeking to make the stent shown in Figures 1 through 4 would take particular care to make the loops of Figures 1 through 4 rounded so as to prevent sharp corners from injuring the inner surface of an artery upon introducing the stent into the vasculature. This is especially true in passing the stent though tortuous vessels when lateral bending of the stent may occur. Additionally, during expansion of the stent, sharp corners could lead to increased injury to the vessel wall and internal elastic lamina (IEL) leading to an increased proliferative response and restenosis.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on February 2nd, 2006 at Washington, D.C.

Jerome Segal, M.D.

Jerome Segal, M.D.

Jerome Segal, M.D.

Education:

College: Wesleyan University, Middletown, CT
1972-1976 Major: Chemistry
Degree: B.A.

Medical School: Tufts University School of Medicine, Boston, MA
1976-1980 Degree: M.D.

Internship & Residency- Internal Medicine:
1980-1983 Harvard University - Beth Israel Hospital, Boston, MA

Fellowship: Division of Cardiology, Stanford University
1983-1986 Medical Center, Stanford, CA

Postdoctoral Fellow in Coronary Interventions:
1986-1987 Director - John B. Simpson, M.D.; Sequoia Hospital,
Redwood City, CA

Academic Appointments:

2002-present Attending, Clinical Instructor- Palo Alto Veterans Administration Hospital
Stanford University
Palo Alto, CA.

2000-2002 Clinical Professor of Medicine
George Washington University
Washington, D.C.

1990-2000 Associate Professor of Medicine (Tenured)
Director, Cardiac Catheterization Laboratories,
George Washington University Medical Center,
Washington, D.C.

1988-1990 Assistant Clinical Professor, Cardiology
University of California, San Francisco;
Director, Cardiac Catheterization Laboratory
San Francisco General Hospital

1987-1988	Clinical Assistant Professor, Cardiology, Stanford University, Veterans Administration Medical Center, Palo Alto, CA
1984-1986	Clinical Specialist, Cardiology Stanford University Medical Center, Stanford, CA

Licenses and Certification:

2002	California State Licensure- renewal
1999	Maryland Medical Licensure
1999	Diplomate, Interventional Cardiology- ABIM
1990	District of Columbia Medical Licensure
1985	Diplomate, Subspecialty of Cardiovascular Disease- ABIM
1983	Diplomate, American Board of Internal Medicine- ABIM
1982	California State Medical Licensure
1981	Massachusetts State Medical Licensure
1981	Diplomate, National Board of Medical Examiners

Employment History:

2005-Present	Founder, President and CEO, Ouroboros, Inc., Mountain View, CA. *Ouroboros has developed a unique spinal implant system for use in total spinal disc replacement and annular reinforcement.*
2000-2005	Founder, President and CEO, Medluminal Systems, Inc., Palo Alto, CA. *Medluminal has developed a unique catheter based drug delivery systems for use in treatment of peripheral vascular disease and as an alternative to drug eluting stents*
1990-2000	Associate Professor of Medicine; Director, Cardiac Catheterization Laboratories, George Washington University, Medical Center, Washington, D.C
1988-1990	Associate Professor of Medicine, Univ. of California, San Francisco Director, Cardiac Catheterization Lab, San Francisco General Hospital
1986-1990	Founder, President and CEO, Cardiometrics, Inc. Mountain View, CA. *Cardiometrics developed and marketed the Flowire for diagnostic use in PTCA. Cardiometrics became a public company in 1990 and was subsequently acquired by Endosonics, Inc.*
1986-1990	Active Staff, Internal Medicine and Cardiology, Sequoia Hospital District, Redwood City, CA;
1983-1986	Attending, Internal Medicine Chope Community Hospital, San Mateo, CA

1981-1983 Attending, Internal Medicine, Bedford Veterans Administration Hospital, Bedford, MA

Honors & Awards

1979 Alpha Omega Alpha, Tufts University School of Medicine
1976-1980 Leopold Schepp Foundation Scholarship; F. August Trust Award; Atlantic Medical Society Award; E. Levinthal Trust Scholarship; Tufts University School of Medicine, Boston, MA
1976 B.A., magna cum laude; Phi Beta Kappa; Sigma Xi; Wesleyan University, Middletown, CT

Professional Organizations

1993 Fellow, Society for Cardiac Angiography and Interventions
1989 Fellow, American College of Cardiology
1983 Member, American College of Physicians;
Member, American Heart Association

Corporate Affiliations

Chairman- Scientific Advisory Board - Interventional Technologies, Inc.
Member - Scientific Advisory Board – Cardiometrics, Inc.

Research Activities

1. Principal Investigator, "Percutaneous Coronary Laser Angioplasty Using the Excimer - 300 Laser System" - George Washington University, participant in multicenter trials.

2. Principal Investigator, "Intracoronary Stenting after failed PTCA, using the Gianturco-Roubin Intracoronary Stent. "George Washington University, participant in multicenter trials.

3. Principal Investigator, "Intracoronary Stenting as a primary adjunct to PTCA, following restenosis." George Washington University, participant in multicenter trials.

4. Principal Investigator - "Effect of local delivery of angiopeptin with a hydrophilic coated balloon angioplasty catheter on atherogenesis." George Washington University.

5. Principal Investigator, "ENDPT" multicenter trial for Doppler intracoronary flowwire measurements performed during PTCA and their

relationship to clinical outcome and restenosis - George Washington University.

6. Principal Investigator, "Correlation of thallium scintigraphy to phasic coronary flow measurements made using a Doppler guidewire." George Washington University.

7. Principal Investigator, "VALID - Velocity Assessment for Lesions of Indeterminant Severity" multicenter trial of medical therapy versus PTCA for lesions measured using the Doppler flowwire." George Washington University.

8. Principal Investigator, "ATLAS - Aspirin Ticlid Anticoagulation for Stents" - Clinical study of abbreviated anticoagulation following stent placement, George Washington University.

9. Principal Investigator, "Evaulation of Free-Flow Perfusion PTCA Balloon in the Treatment of Atherosclerotic Lesions". George Washington University.

10. Principal Investigator, Fullflow Mechanical Dilation Spring Catheter", animal trials of new angioplasty catheter for FDA-IDE submission, George Washington University.

11. Co-investigator, Assessment of Coronary collateral flow using a Doppler guidewire." St. Louis University and George Washington University.

Dr. Morton Kern - Principal Investigator.

12. Co-investigator, "Significance of intermediate coronary artery lesions." St. Louis University and George Washington University.

Dr. Morton Kern - Principal Investigator.

13. Co-investigator, "Global utilization of Streptokinase and t-PA for occluded coronary arteries (GUSTO)." Angiographic Core Laboratory. George Washington University.

14. Co-investigator, "Multi-center American research trial with cilzapril after angioplasty to prevent transluminal coronary obstruction and restenosis (Marcator)." George Washington University.

15. Co-investigator "Insulin and Pathogenesis of Atherosclerosis in Blacks" NIH92HLIH.

16. Co-investigator "A multicenter, double blind, randomized study to compare safety and efficacy of BG8967 with Heparin in patients undergoing PTCA."

17. Director, Quantitative angiographic core laboratory for Strucker coronary artery stent, multicenter trials.

18. Director, Quantitative angiographic core laboratory for VALID and ENDPT, multicenter trials for Doppler flowwire measurements during PTCA.

19. Research Supervisor to six George Washington University Cardiology research fellows: Studies including:

a. "Coronary geometry and its relationship to phasic coronary artery flow velocity patterns" - recipient 1993-Squib Diagnostics/SCA & I Fellowship Program Grant."

b. "Relationship of coronary flow patterns to regional myocardial function" 1992 American Heart Association, Research Fellowship Grant

c. "Relationship of phasic coronary artery flow patterns to thallium scintigraphy in patients undergoing Cardiac catheterization" Merck Research Fellowship Grant

d. "Effect of femoral-femoral cardiopulmonary bypass on left ventricular dysfunction and coronary flow after myocardial infarction" American Heart Association, Research Fellowship Grant.

e. "Relationship of Coronary flow patterns to regional myocardial function with dobutamine following angioplasty." American Heart Association, Research Fellowship Grant -

f. "Combined use of the instantaneous diastolic hyperemic flow velocity versus pressure slope index and intracoronary ultrasound to assess the adequacy of coronary angioplasty. (SCAI - Fellowship Grant- Application

g. "Clinical Evaluation of Doppler Determined Coronary Artery Flow Parameters in Acute Myocardial Infarction with Tc-Sestamibi Imaging", SCAI - Fellowship Grant- Application

Sponsor or Principal Investigator

American Heart Association, Washington Branch, post doctoral research fellowship grant (Yuri Deychak) . Animal research proposal to study the relationship of changes in coronary artery flow patterns and regional myocardial function.

Society for Cardiac Angiography and Interventions - post doctoral research fellowship grant (John Reiner) . Animal research project to study the effect of lesion geometry on coronary flow obstructions and changes in distal coronary artery flow parameters.

Boston Scientific Corporation, Strecker Intracoronary Stent - Database establishment and presentation of Strecker multicenter data, grant.

Winthrop Fellowship Grant, gift grant from Winthrop pharmaceuticals to fund senior interventional fellow at George Washington.

ENDPT - multicenter Doppler coronary flow trial - angiographic core laboratory, approximately 500 angiograms.

Terumo Angioplasty Glidewire, prototype development and testing in the animal laboratory..

Mansfield Synergy Perfusion Balloon, development and animal testing, estimated grant.

Schneider, Inc. Development and animal testing of a new perfusion balloon catheter.

Interventional Technologies, Inc. Animal Studies of new mechanical dilatation catheter for FDA-IDE submission for human use.

Co-Investigator

ATLAS - "Aspirin/Ticlid Anticoagulation for Stents", Clinical study of reduced anticoagulation following stent placement, Sponsor - Hoffmann-LaRoche.

GUSTO - "Global Utilization of Streptokinase and t-PA for occluded coronary arteries." Angiographic Core Laboratory.

MARCATOR - "Multi-center American Research trial with cilazapril after angioplasty to prevent transluminal coronary obstruction and restenosis".

BIOGEN Corporation - "Multi-center, double blind, randomized study to compare the safety and efficacy of BG8967 with Heparin in patients undergoing PTCA".

PACT - "Plasminogin Activator Angioplasty Compatibility Trial", multicenter clinical trial of angioplasty versus thrombolysis for acute MI.
Sponsor – Genentech.

Publications

1. Segal J, Cardiac Output obtained with a Doppler pulmonary artery catheter. JACC 1989; 13:1382-1392.

2.Segal J, Nassi M, Ford AJ: Instantaneous and continuous cardiac output in man using a Doppler pulmonary artery catheter. JACC 1990; 16:1398-1407.

3.Segal J, Guadiani V, Nishimura T: Continuous determination of cardiac output using a flow directed Doppler pulmonary catheter. JL Cardiothor Anesth 1991:5;No.4:309-15.

4.Segal J, Kern MJ, Scott NA, Docette JW, Heuser RR, Ofili E, Siegel R: Alterations of phasic coronary artery flow velocity in man during percutaneous coronary angioplasty. JACC 1992:20:276-86

5.Ardehali A, Segal J , Cheitlin MD: An improved valve-spreading catheter for producing reversible graded acute aortic insufficiency. Am Jl Phsiol;; 1987 (in press)

6.Doucette JW, Corl PD, Payne HM, Flynn AE, Goto M, Nass M, Segal J: Validation of a Doppler Guidewire for Intravascular measurement of coronary artry flow velocity Circulation 1992; 85:1899-1911.

7.Segal J. Lundergan CF: Determination of the hemodynamic significance of coronary artery stenoses of intermediate severity. Am Heart Jl 1992; 124:1073-77.

8.Segal J, Applications of coronary flow velocity during angioplasty and other coronary interventional procedures. Am Jl..Cardiol. 1993; 71:17D-25D.

9.Kern MJ, Aguirre F, Bach R, Donogue T, Segal J: Augmentation of coronary blood flow by intra-aotic balloon pumping in patients after coronary angioplasty. Circulation. 1993; 87:500-511.

10.Thompson MA, Deychalk YA, Segal J: Doppler-tipped guidewire assessment of retrograde coronary artery flow distal to a total occlusion and its reversal following laser recanalization. Am. Heart Jl. 1993; 125:526-530.

11.Ofili EQ, Labovitz AJ, Kern MJ, St. Vrain JA, Segal J, Aguirre F, Castello R: Analysis of coronary blood flow velocity dynamics in angiographically normal and stenosed arteries before and after endoluminal enlargement by angioplasty. JACC 1993; 21:308-16.

12.Donohue TJ, Kern MJ, Aguirre FV, Bach RG, Wolford T, Bell C, Segal J: Assessing the significance of coronary artery stenoses: analysis of translesional pressure-flow velocity relationships in patients. JACC 1993; 22:449-58.

13.Maldowney WP, Humphreys MH, Segal J: the diagnosis of Cardiac Tamponade in endstage renal disease patients. Submitted.

14.Deychak YA, Segal J, Thompson MA, Rohrbeck SC, Mukherjee A, Herzog WR, Lundergan CF: A Doppler guidewire used to assess coronary flow during directional coronary atherectomy

15.Deychak YA, Segal J, Reiner JS, Nachnani S: Doppler guidewire derived coronary flow reserve distal to intermediate stenoses utilized in clinical decision-making regarding interventional therapy. Am. Heart Jl. 1994; 128: 178-81.

16.Ardehali A, Segal J. Cheitlin MD: Coronary flow reserve in acute aortic regurgitation JACC (In press).

17.Deychak YA, Segal J, Reiner JS, Rohrbeck SC, Thompson MA, Lundergan CF, Ross AM, Wasserman AG: Doppler guide wire flow-velocity indexes measured distal to coronary stenoses associated with reversible thallium perfusion defects. Am. Heart Jl. 1995; 129:219-27.

18.Borenstein D, Jenkins E, Cho S, Segal J, Ross A: The prevalence of low back pain and theraeutic requirements of interventional cardiologists, orthopedic surgeons, and rheumatologists: A possible relationship with lead aprons. Am J. Cardiol. 1997; 79:68-70.

19.Moreyra, Segal J, Taheri H, Beohar N: Coronary flow in a patient with coronary ectasia and hypertrophic cardiomyopathy (In-Press).

20.Segal J, Wolinsky SC, Sunew J, Lopez A, Moreyra E: Coronary angioplasty performed using the FullFlow mechanical dilatation-perfusion catheter; initial animal experience.Cath. and Cardiovasc. Int. 2000;

21. Segal J, Scott NA, Hampikian J: Supression of proliferative response following PTCA using a new Beta radiation catheter system- submitted

22. Segal J, Scott NA: Catheter-based iontophoretic local drug delivery of a novel DNA compound - submitted

Book Chapters:

1. The Doppler Guidewire: A new method to evaluate coronary artery flow during percutaneous trnsluminal coronary angioplasty - in Vogel: The practice of Interventional Cardiology/Second Edition. Mosby -1992.

2. Segal J, Moreyra E: Comparative Utility of Intravascular Ultrasound versus the doppler flow wire in diagnostic decision-making in coronary artery disease. Chapter 9, Ultrasound Imaging in Coronary Artery Disease, Robert J. Siegel: Marcel Decker - New York,-1997.

Patents:

1. Segal J: Blood Flow Measurement Catheter (4,733,669, March 29, 1988).

2. Segal J: Ultrasonic Pulmonary Artry Catheter and Method (4,856,529, Aug.15, 1989).

3. Segal J, Corl PD, Hasse WC: Device and Method for Measuring Volumetric Blood Flow in a Vessel (4,869,263, Sept. 26, 1989).

4.Hasse WC, Segal J, Corl PD, Christian J, Williams R: Apparatus, System and Method for Measuring Spatial Average Velocity and/or Volumetric Flow of blood in a Vessel; (4,967,753, Nov. 6, 1990).

5. Nasi M, Corl PD, Williams R., Cowan M. Segal J: Apparatus and Method for Continuously Measuring Columetric Blod Flow Using Multiple Transducers and Catheter for Use Therewith (4,947,852, Aug. 14, 1990).

6. Christian J. Corl PD, Segal J, Williams R, Hasse WC: Apparatus, System and Method for Measuring Spatial Average Velocity and/or Volumetric Flow of Blood in a Vessel (4,967,753, Nov. 6, 1997.

7. Segal J: Vascular Dilatation, Device and Method (5,527,282 June 18, 1996).

8. Segal J: Vascular Dilatation, Device and Method (8,509,579 Dec. 8, 1995).

9. Segal J: Mechanical Apparatus and Method for Deployment of Expandable Prosthesis (5,755,709 May 26, 1998).

10. Segal J: Mechanical Apparatus and Method for Dilating and Irradiating a Site of Treatment (6,059,752 May 9, 2000).

11. Yurek M, Olson T, Segal J: Apparatus and Method for Deployment of an Expandable Prosthesis having Calibrated and Longitudinally Incompressible Expansion Means (filed Sept. 1999, later abandoned.

12. Segal J, Hampikian JM, Scott NA: Device and Method for Dilating and Irradiating a Vascular Segment or Body Passageway (US PTO App# 09/735,239)

13. Segal J, Scott NA: Mechanical Apparatus and Method for Dilating and Delivering a Therapeutic Agent to a Site of Treatment (US-PTO App#10/135,709)

14. Segal J, Scott NA: Mechanical Apparatus and Method for Dilating and Delivering a Therapeutic Agent to a Site of Treatment- (US-PTO App# 09/997/855)

15. Scott NA, Segal J: Charged Liposomes/Micelles with Encapsulated Medical Compounds (US-PTO App#10/214,959)

16. Segal J, Scott NA: Polymer Coated Device for Electrically Mediated Drug Delivery (US-PTO App# 10/425,170)

17. Scott NA, Segal J: Mechanical Apparatus and Method for Dilating and Delivering a Therapeutic Agent (US-PTP App# 60/580,680)

18. Segal J, Scott NA: Apparatus and Method for Dilating and Delivering a Therapeutic Agent to a Treatment Site (US-PTO App# 10/951964)

19. Segal J, Scott NA, Harris S: High Concentration Medicament and Polymer Coated Device for Passive Diffusional Medicament Delivery (US-PTO App# 11/027326)

20. Segal J, Yurek M: Mechanical Apparatus and Method for Artificial Disc Replacement (US-PTO App# 11/153,776)

21. Segal J, Yurek M: Mechanical Apparatus and Method for Artificial Disc Replacement (US-PTO App# 11/173,034)

22. Segal J, Yurek M, Yuan H, Yeung A: Mechanical Apparatus and Method for Artificial Disc Replacement (US-PTO App# 11/273,299)

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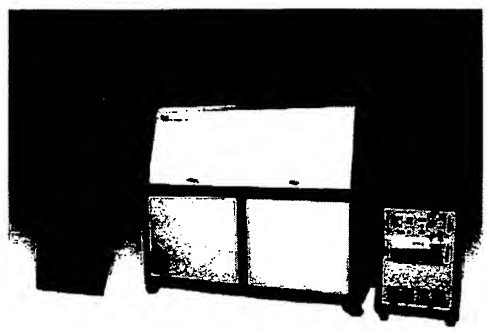

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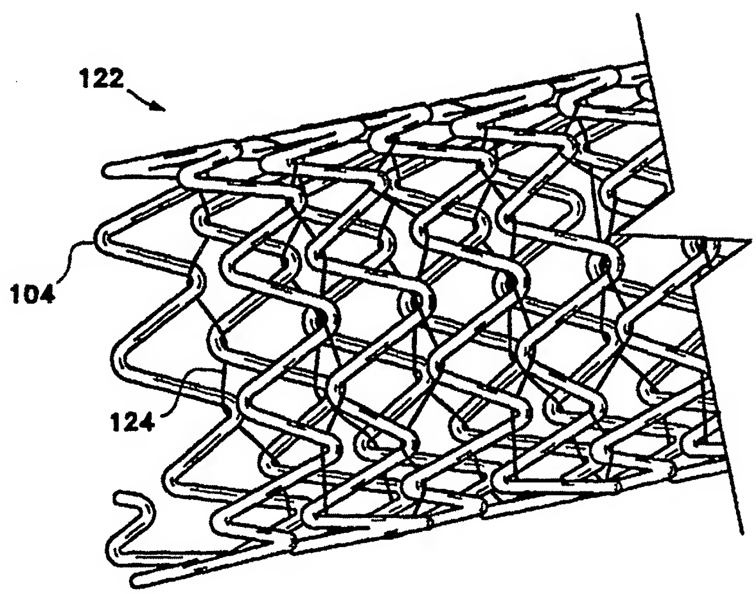
(57) Abstract

The device is a foldable stent (122) or stent-graft (370) which may be delivered with (or on) a catheter or via surgical or other suitable techniques. The device is then expanded or unfolded. The expandable stent structure preferably utilizes at least one torsional member (100) generally aligned with the longitudinal axis of the stent (122). The stent (122) preferably has an undulating shape. It may be helically deployed to form the generally cylindrical shape eventually deployed as the stent (122) or it may be formed of one or more rings (302). The structure desirably is aligned to allow those undulating shapes in adjacent rings (322) or turns of the helix to be in phase. The adjacent undulating shapes may be held in that phased relationship using a flexible linkage (324) often made of a polymeric material. The stent (122) is self-expanding, kink-resistant, easily bent along its longitudinal axis, does not change its length during that expansion, and is able to provide collapsible support for otherwise frangible graft material. The graft component (134) cooperating with the stent (122) is tubular and may be a biocompatible polymeric or collagenous material or combinations of the two which may, if desired, be reinfored with fibers.



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SELF-EXPANDABLE STENT AND STENT-GRAFT AND METHOD OF USING THEM

FIELD OF THE INVENTION

This invention is a medical device and a method of using it. The device is a foldable stent or stent-graft which may be delivered with (or on) a catheter or via surgical or other suitable techniques. The device is then expanded or unfolded. The expandable stent structure preferably utilizes at least one torsional member generally aligned with the longitudinal axis of the stent. The stent preferably has an undulating shape. It may be helically deployed to form the generally cylindrical shape eventually deployed as the stent or it may be formed of one or more rings. The structure desirably is aligned to allow those undulating shapes in adjacent rings or turns of the helix to be in phase. The adjacent undulating shapes may be held in that phased relationship using a flexible linkage, often made of a polymeric material. The stent's configuration allows it to be folded or otherwise compressed to a very small diameter prior to deployment without changing the length of the stent. The stent is self-expanding, kink-resistant, easily bent along its longitudinal axis, does not change its length during that expansion, and is able to provide collapsible support for otherwise frangible graft material. The graft component cooperating with the stent is tubular and may be a biocompatible polymeric or collagenous material or combinations of the two which may, if desired, be reinforced with fibers.

The invention involves procedures for deploying stents or stent-grafts which have been folded, bound, or

otherwise collapsed to significantly smaller diameters for insertion into a human or animal body. The deployment procedures may involve the use of an outer sleeve to maintain the stent or stent-graft at a reduced diameter or may involve a "slip-line" to hold and then to release the device.

BACKGROUND OF THE INVENTION

With the advent of interventional radiology, the treatment or isolation of a variety of maladies in he body's conduits may be easily treated using stents and stent-grafts. For instance, this invention may be used to treat weakened, distorted, narrowed, or otherwise malformed vessels in the vascular, biliary, genito-urinary, gastrointestinal, and respiratory systems. Of special interest in the use of this invention is the treatment of vascular aneurysms or of arterial or venous vessel walls which have been thinned or thickened by disease. Much of this vascular treatment has traditionally been done via surgery, e.g., via the use of surgical bypassing with vascular grafts. Shortcomings of this procedure include the morbidity and mortality associated with surgery, long recovery times after surgery, and the high incidence of repeat intervention needed due to limitations of the graft or of the procedure. Vessels thickened by disease are currently sometimes treated less invasively with intraluminal stents that mechanically hold these vessels open either subsequent to or as an adjunct to a balloon angioplasty procedure. Shortcomings of current stents as used in the vascular system include the use of highly thrombogenic materials (stainless steels, tantalum, ELGILOY) which are exposed to blood, the general failure of these materials to attract and support functional endothelium, the

irregular stent/vessel surface that causes unnatural blood flow patterns, and the mismatch of compliance and flexibility between the vessel and the stent.

Highly desirable in this invention is the use of less invasive intraluminal delivery and, in a preferred aspect when used in the vascular system, placement of a nonthrombogenic blood-carrying conduit having a smooth inner lumen which will endothelize.

A desirable graft material chosen for the inner layer of the inventive stent-graft is collagen-based and, although it will fold with ease, is otherwise fairly frangible or inelastic in that it has very little ability to stretch. Mounting a collagen tube on the outside of or as a part of a balloon-expandable stent will usually cause the tube to tear. Mounting such a tube on the inside of a balloon expandable stent will yield a torn irregular surface exposed to blood flow. Further, balloon expandable devices that rely upon plastic deformation of the stent to achieve a deployed shape are subject to abrupt closure as a result of trauma when the devices are placed in a vessel near the skin surface or across a joint or ligament. Those self-expanding stents which rely on the shortening of the stent upon radial expansion at deployment may cause vessel tearing problems similar to those observed with the use of balloon expandable devices. Obviously, stents which shorten during deployment are also subject to deployment placement inaccuracies.

The most desired variations of this invention involve a stent-graft which is self-expanding, which does not shorten upon delivery, which has excellent longitudinal flexibility, which has high radial compliance to the vessel lumen, and exposes the blood to

a smooth, nonthrombogenic surface capable of supporting endothelium growth.

The inventive device may be delivered in a reduced diameter and expanded to maintain the patency of any conduit or lumen in the body, particularly those mentioned above. An area in which the inventive stent and stent graft is particularly beneficial is in the scaffolding of atherosclerotic lesions in the cardiovascular system to establish vessel patency, prevention of thrombosis, and the further prevention of re-stenosis after angioplasty. In contrast to many of the stents discussed below having metallic struts intruding into the blood flow in the vessel lumen which generate turbulence and create blood stasis points initiating thrombus formation, the smooth, continuous surface provided by the tubular collagen-based, polymer-based, or combination inner conduit of our invention provides a hemodynamically superior surface for blood flow.

The non-thrombogenic properties of an sPEG collagen surface results in a less thrombogenic device. Clinically, this allows a more moderate anti-coagulation regimen to be used. As a result, the rate of bleeding complications, a major drawback associated with stenting, may be reduced. The absence of gaps or holes in the graft structure between stent struts of our invention allows the tacking of both large and small flaps and tears in the vessel wall. These flaps disrupt blood flow and attract thrombus. The disruption of the natural anti-thrombotic covering of endothelium only worsens the condition. The collagen-based barrier we interpose between blood and a disrupted or injured portion of the vessel wall serves to mask injured intimal or medial layers from blood, thereby preventing thrombus formation

and intimal proliferation which may lead to re-stenosis.

The presence of our inventive stent-graft acts as a mechanical barrier preventing tissue from proliferating into or impinging the lumen. The nature of the bioactivity of the collagen and the smoother flow characteristics at the blood-contacting surface are conducive to endothelial cell attachment and growth thereby assuring the long-term blood compatibility of the device.

Mechanically, our stent structure provides a good combination of radial strength and flexibility. The structure is also radially resilient. It can be completely crushed or flattened and yet spring open again once the obstructive loading is removed. This ability is important for use in exposed portions of the body around the peripheral vasculature or around joints. The stent-graft can sustain a crushing traumatic blow or compression from the bending of a joint and still return to the open configuration once the load is removed.

With regard to delivery, the self-expansion mechanism eliminates the need for a balloon catheter and the associated balloon rupture problems often associated with balloons. In addition, the absence of the bulk of the balloon allows a smaller delivery profile to be achieved. Unlike some other self-expanding stent designs, this stent-graft maintains a constant length throughout the expansion process. Thus, the stent-graft would not have some of the positioning problems associated with other many self-expanding stents. In treating longer lesions, our self-expanding design eliminates the need for special long balloons or repositioning of the balloon between inflations in order to expand the entire length of the stent.

When used as a conventional vascular graft or intraluminal graft, our collagen-based stent-grafts offer a number of advantages over existing technologies. Unlike expanded polytetrafluoroethylene (PTFE) grafts, the bare collagen-based material supports endothelial cell growth and is incorporated into the surrounding tissue. As an intraluminal graft, the device has several advantages. The wall thickness may be made thinner than tanned, reinforced biologic grafts. When placed inside the lumen of a vessel, a thin-walled graft results in a larger opening for blood flow resulting in improved hemodynamics. Lastly, when used as an intraluminal graft, there is no anastomosis site. Anastomosis sites are thought to be a common source of problems associated with graft failures.

The impermeability of the inventive stent-graft makes it suitable for shunting and thereby hydraulically isolating aneurysms. The expansile properties derived from the stent structure provide a secure anchor to the vessel wall. The stent reinforces frangible graft materials making up the tubular component thereby increasing the overall burst strength of the stent-graft.

Finally, the organic composition of the collagen-based materials which may be used in the inventive stent-graft provides an excellent vehicle for localized drug delivery. In addition, therapeutic compounds may be linked, conjugated, or otherwise more easily bound to the organic graft material (or to its substituents, such as PEG) than to the surface of a metallic structure. Localized drug delivery is desirable in preventing thrombosis or re-stenosis. Therapeutically effective doses may be administered to the target area without systemic concentrations being raised. This

capability is of great benefit in reducing side-effects and complications associated with drug therapy.

Therapeutic agents may be delivered out of the collagen matrix by diffusion. Alternatively, these agents may be bound temporarily or permanently on the collagen surfaces. Different agents may be bound on the inner and outer surfaces to achieve different therapeutic ends. For example, a drug to minimize thrombus formation might be appropriate for the inside, blood-contacting surface, while a drug which would inhibit smooth muscle cell proliferation might be appropriate on the outer surface. Drugs can be chemically or physically bound to either the sPEG or the collagen molecules.

Stents

The stents currently described in the open literature include a wide variety of different shapes.

Wallsten, U.S. Patent No. 4,655,771, suggests a vascular prosthesis for transluminal implantation which is made up of a flexible tubular body having a diameter that is varied by adjusting the axial separation of the two ends of the body relative to each other. In general, the body appears to be a woven device produced of various plastics or stainless steel.

U.S. Patent No. 4,760,849, to Kroph, shows the use of a ladder-shaped coil spring which additionally may be used as a filter in certain situations.

Porter, U.S. Patent No. 5,064,435, suggests a stent made up of two or more tubular stent segments which may be deployed together so to produce a single axial length by a provision of overlapping areas. This concept is to permit the use of segments of known length, which, when deployed, may be used together in overlapping

fashion additively to provide a stent of significant length.

Quan-Gett, U.S. Patent No. 5,151,105, discloses an implantable, collapsible tubular sleeve apparently of an outer band and an inner spring used to maintain the sleeve in a deployed condition.

Wall, U.S. Patent No. 5,192,307, suggests a stent having a number of holes therein and which is expandable using an angioplasty balloon so to allow ratchet devices or ledges to hold the stent in an open position once it is deployed.

The following patents use wire as the stent material.

Gianturco, in U.S. Pat. Nos. 4,580,568 and 5,035,706, describes stents formed of stainless steel wire arranged in a closed zigzag pattern. The stents are compressible to a reduced diameter for insertion into and removal from a body passageway. The stents appear to be introduced into the selected sites by discharge of the collapsed zigzag wire configuration from the tip of a catheter.

U.S. Patent Nos. 4,830,003 and 5,104,404, to Wolff et al., shows a stent of a zigzag wire configuration very similar in overall impression to the Gianturco device. However, the stent is said to be self-expanding and therefore does not need the angioplasty balloon for its expansion.

Hillstead, U.S. Patent 4,856,516, suggests a stent for reinforcing vessel walls made from a single elongated wire. The stent produced is cylindrical and is made up of a series of rings which are, in turn, linked together by half-hitch junctions produced from the single elongated wire. It is not helically wound, nor is there

a second linking member tending to link the helices together.

Wiktor, U.S. Patent Nos. 4,649,992, 4,886,062, 4,969,458, and 5,133,732, shows wire stent designs using variously a zigzag design or, in the case of Wiktor '458, a helix which winds back upon itself. Wiktor '062 suggests use of a wire component made of a low-memory metal such as copper, titanium or gold. These stents are to be implanted using a balloon and expanded radially for plastic deformation of the metal.

Wiktor '458 is similarly made of low-memory alloy and is to be plastically deformed upon its expansion on an angioplasty balloon.

Wiktor '732 teaches the use of a longitudinal wire welded to each turn of the helically wound zig-zag wire which is said to prevent the longitudinal expansion of the stent during deployment. A further variation of the described stent includes a hook in each turn of the helix which loops over a turn in an adjacent turn. Neither variation includes a flexible linkage between adjacent helices.

WO93/13825, to Maeda et al, shows a self-expanding stent similar to the Gianturco, Wolff, and Wiktor designs, formed of stainless steel wire, which is built into an elongated zig-zag pattern, and helically wound about a central axis to form a tubular shape interconnected with a filament. The bends of the helix each have small loops or "eyes" at their apexes which are inter-connected with a filament. Because of the teaching to connect the eyes of the apexes, the stent appears to be a design that axially expands during compression and may tear attached grafts because of the relative change in position of the arms of the zig-zag during compression of the stent.

MacGregor, U.S. Pat. No. 5,015,253, shows a tubular non-woven stent made up of a pair of helical members which appear to be wound using opposite "handedness". The stent helices desirably are joined or secured at the various points where they cross.

Pinchuk, in U.S. Pat. Nos. 5,019,090, 5,092,877, and 5,163,958, suggests a spring stent which appears to circumferentially and helically wind about as it is finally deployed except, perhaps, at the very end link of the stent. The Pinchuk '958 patent further suggests the use of a pyrolytic carbon layer on the surface of the stent to present a porous surface of improved antithrombogenic properties. The helices are not linked to each other, however, nor is there any suggestion that the helices be maintained in a specific relationship either as deployed or as kept in the catheter prior to deployment.

U.S. Patent No. 5,123,917, to Lee, suggests an expandable vascular graft having a flexible cylindrical inner tubing and a number of "scaffold members" which are expandable, ring-like, and provide circumferential rigidity to the graft. The scaffold members are deployed by deforming them beyond their plastic limit using, e.g., an angioplasty balloon.

Tower, in U.S. Pat. Nos. 5,161,547 and 5,217,483, shows a stent formed from a zig-zag wire wound around a mandrel in a cylindrical fashion. It is said to be made from "a soft platinum wire which has been fully annealed to remove as much spring memory as possible." A longitudinal wire is welded along the helically wound sections much in the same way as was the device of Wiktor.

There are a variety of disclosures in which super-elastic alloys such as nitinol are used in stents.

See, U.S. Patent Nos. 4,503,569, to Dotter; 4,512,338, to Balko et al.; 4,990,155, to Wilkoff; 5,037,427, to Harada, et al.; 5,147,370, to MacNamara et al.; 5,211,658, to Clouse; and 5,221,261, to Termin et al. None of these references suggest a device having discrete, individual, energy-storing torsional members as are required by this invention.

Jervis, in U.S. Pat. Nos. 4,665,906 and 5,067,957, describes the use of shape memory alloys having stress-induced martensite properties in medical devices which are implantable or, at least, introduced into the human body.

<u>Stent-Grafts</u>

A variety of stent-graft designs are shown in the following literature.

Perhaps the most widely known such device is shown in Ersek, U.S. Pat. No. 3,657,744. Ersek shows a system for deploying expandable, plastically deformable stents of metal mesh having an attached graft through the use of an expansion tool.

Palmaz describes a variety of expandable intraluminal vascular grafts in a sequence of patents: U.S. Patent Nos. 4,733,665; 4,739,762; 4,776,337; and 5,102,417. The Palmaz '665 patent suggests grafts (which also function as stents) that are expanded using angioplasty balloons. The grafts are variously a wire mesh tube or of a plurality of thin bars fixedly secured to each other. The devices are installed, e.g., using an angioplasty balloon and consequently are not seen to be self-expanding.

The Palmaz '762 and '337 patents appear to suggest the use of thin-walled, biologically inert

materials on the outer periphery of the earlier-described stents.

Finally, the Palmaz '417 patent describes the use of multiple stent sections each flexibly connected to its neighbor.

Rhodes, U.S. Pat. No. 5,122,154, shows an expandable stent-graft made to be expanded using a balloon catheter. The stent is a sequence of ring-like members formed of links spaced apart along the graft. The graft is a sleeve of a material such as expanded polyfluorocarbon, e.g., GORETEX or IMPRAGRAFT.

Schatz, U.S. Pat. No. 5,195,984, shows an expandable intraluminal stent and graft related in concept to the Palmaz patents discussed above. Schatz discusses, in addition, the use of flexibly-connecting vascular grafts which contain several of the Palmaz stent rings to allow flexibility of the overall structure in following curving body lumen.

Cragg, "Percutaneous Femoropopliteal Graft Placement", <u>Radiology</u>, vol. 187, no. 3, pp. 643-648 (1993), shows a stent-graft of a self-expanding, nitinol, zig-zag, helically wound stent having a section of polytetrafluoroethylene tubing sewed to the interior of the stent.

Cragg (European Patent Application 0,556,850) discloses an intraluminal stent made up of a continuous helix of zig-zag wire and having loops at each apex of the zig-zags. Those loops on the adjacent apexes are individually tied together to form diamond-shaped openings among the wires. The stent may be made of a metal such as nitinol (col. 3, lines 15-25 and col. 4, lines 42+) and may be associated with a "polytetrafluoroethylene (PTFE), dacron, or any other suitable biocompatible material". Those biocompatible

materials may be inside the stent (col. 3, lines 52+) or outside the stent (col. 4, lines 6+). There is no suggestion that the zig-zag wire helix be re-aligned to be "in phase" rather than tied in an apex-to-apex alignment. The alignment of the wire and the way in which it is tied mandates that it expand in length as it is expanded from its compressed form.

Grafts

As was noted above, the use of grafts in alleviating a variety of medical conditions is well known. Included in such known grafting designs and procedures are the following.

Medell, U.S. Patent No. 3,479,670, discloses a tubular prothesis adapted to be placed permanently in the human body. It is made of framework or support of a synthetic fiber such as DACRON or TEFLON. The tube is said to be made more resistant to collapse by fusing a helix of a polypropylene monofilament to its exterior. The reinforced fabric tube is then coated with a layer of collagen or gelatin to render the tubing (to be used as an esophageal graft) impermeable to bacteria or fluids.

Sparks, in U.S. Patent Nos. 3,514,791, 3,625,198, 3,710,777, 3,866,247, and 3,866,609, teach procedures for the production of various graft structures using dies of suitable shape and a cloth reinforcing material within the die. The die and reinforcement are used to grow a graft structure using a patient's own tissues. The die is implanted within the human body for a period of time to allow the graft to be produced. The graft is in harvested and implanted in another site in the patient's body by a second surgical procedure.

Braun, in U.S. Patent No. 3,562,820, shows a biological prosthesis manufactured by applying onto a

support of a biological tissue (such as serosa taken from cattle intestine) a collagen fiber paste. The procedure is repeated using multiple layers of biological tissue and collagen fiber paste until a multi-layer structure of the desired wall thicknesses is produced. The prosthesis is then dried and removed prior to use.

Dardik et al, U.S. Patent No. 3,974,526, shows a procedure for producing tubular prostheses for use in vascular reconstructive surgeries. The prosthesis is made from the umbilical cord of a newly born infant. It is washed with a solution of 1 percent hydrogen peroxide and rinsed with Ringer's lactate solution. It is then immersed in a hyaluronidase solution to dissolve the hyaluronic acid coating found in the umbilical cord. The vessels are then separated from the cord and their natural interior valving removed by use of a tapered mandrel. The vessels are then tanned with glutaraldehyde. A polyester mesh support is applied to the graft for added support and strength.

Whalen, U.S. Patent No. 4,130,904, shows a prosthetic blood conduit having two concentrically associated tubes with a helical spring between them. Curved sections in the tube walls help prevent kinking of the tube.

Ketharanathan, U.S. Patent No. 4,319,363, shows a procedure for producing a vascular prosthesis suitable for use as a surgical graft. The prosthesis is produced by implanting a rod or tube in a living host and allowing collagenous tissue to grow on the rod or tube in the form of coherent tubular wall. The collagenous implant is removed from the rod or tube and tanned in glutaraldehyde. The prosthesis is then ready for use.

Bell, U.S. Patent No. 4,546,500, teaches a method for making a vessel prosthesis by incorporating a

contractile agent such as smooth muscle cells or platelets into a collagen lattice and contracting the lattice around a inner core. After the structure has set, additional layers are applied in a similar fashion. A plastic mesh sleeve is desirably sandwiched between the layers or imbedded within the structure to provide some measure of elasticity.

Hoffman Jr. et al, U.S. Patent No. 4,842,575, shows a collagen impregnated synthetic vascular graft. It is made of a synthetic graft substrate and a cross-linked collagen fibril. It is formed by depositing a aqueous slurry of collagen fibrils into the lumen of the graft and massaging the slurry into the pore structure of the substrate to assure intimate admixture in the interior. Repeated applications and massaging and drying is said further to reduce the porosity of the graft.

Alonoso, U.S. Patent No. 5,037,377, is similar in overall content to the Hoffman Jr. et al patent discussed above except that, in addition to collagen fibers, soluble collagen is introduced into the fabric. A suitable cross-linking agent such as glutaraldehyde is used to bond adjacent collagen fibers to each other.

Slepian et al, U.S. Patent No. 5,213,580, teaches a process described as "paving" or "stabilizing by sealing the interior surface of a body vessel or organ" by applying a biodegradable polymer such as a polycaprolactone. The polymer is made into a tubular substrate, placed in position, and patched into place.

Finally, there are known vascular grafts using collagenous tissue with reinforcing structure. For instance, Pinchuk, in U.S. Patent Nos. 4,629,458 and 4,798,606, suggests the use of collagen with some other type of fibrous structure supporting the collagen as a biograft. Similarly, Sinofsky et al., U.S. Pat. No.

5,100,429, suggests a partially-cured, collagen-based material used to form a graft within a blood vessel.

Kreamer, U.S. Pat. No. 4,740,207, suggests a intraluminal graft made of a semi-rigid resilient tube, open along a seam extending from one end to the other, which is expanded within the vessel and which resulting larger diameter is maintained by use of a ledge at the longitudinal seam for catching the opposite side of the seam on the expanded graft.

We have found that elasticity, or the ability of a material to return to its original shape after a deformation, can be maintained in smaller stents by the distribution of folding deformation throughout the structure. By incorporating hinges or hinge regions into the structure, the distribution of "localized" folding deformation is maximized. The hinge regions include torsion members allowing a significant portion of the folding displacement to be re-oriented parallel to the longitudinal axis of the stent-graft. The act of folding, crushing, or otherwise elastically deforming the stent creates a significant torsional component in the torsion members which component is parallel to that longitudinal axis. The hinges are positioned at least at each of the fold points around the circumference of the stent where folding is desired. The circumferentially oriented regions of the stents, which connect the torsion members, pivot about the torsion members, causing the torsion members to undergo a twisting deformation. In order to avoid exceeding the elastic limit of the material, the length of the torsion members is increased to lower the amount of twist per length or strain imposed. The orientation of the torsion members is such that their length does not increase the circumference of

the device. None of the cited references suggest such a device.

SUMMARY OF THE INVENTION

This invention is a foldable stent or stent-graft which may be percutaneously delivered through or over a catheter or using surgical techniques or other appropriate methodologies. The expandable stent structure utilizes torsional regions which allow it to be folded to a very small diameter prior to deployment without significant deformation. The torsional members may have an undulating shape which may be helically deployed to form the stent's cylindrical shape. The torsional members may also be found in one or more rings spaced axially along the stent. It may be helically deployed to form the generally cylindrical shape eventually deployed as the stent or it may be formed of one or more rings. The undulating shape may be aligned to allow the shapes in adjacent turns of the helix to be in phase. The undulating shapes may be generally V-shaped, U-shaped, sinusoidal, or ovoid. Adjacent undulating shapes may be held in the phased relationship using a flexible linkage, often made of a polymeric material. The undulating torsional members typically will not have any means at (or near) the apex of the undulating shapes which would tend to constrict the movement of the flexible linkage during compression of the stent. The stent may be expanded with the use of an installation device such as an angioplasty balloon but preferably is used as a self-expandable device.

The graft component used to complement the stent may be tubular if such a form is needed to correspond to the shape of the stent and the vessel. One desirable stent material is collagenous material which

may, if desired, be reinforced with fibers of random, woven, roving, or wound configurations. The graft member may be cast onto or otherwise attached or imbedded into the stent structure. The stent-graft may be used to reinforce vascular irregularities and provide a smooth interior vascular surface, particularly within smaller vessels. Other vessels are also suitably used with collagenous grafts.

The graft component may also be a polymeric material which may be attached variously to the filament used to maintain the shape of the stent structure (when such filament is used) or to the stent structure itself. The graft component desirably is a biocompatible, expanded polyfluoroethylene polymer tubular component. Highly desirable is a graft component comprised of an expanded porous polymeric tubing having collagenous material embedded in the pores of the polymeric tubing. The attachment between the graft component and the stent, e.g., by bonding the graft component to the flexible linkage or by using eyelets or other discrete or continuous linking sites, is desirably crafted to allow the stent torsional members to slide longitudinally with respect to each other and to the graft component and so maintain the interior shape of graft. This is to say that the graft component is supported at a variety of sites located along its outer surface. Bending the stent-graft combination distributes the flexing movement of the graft over a long region because of the distributed support of the stent. The tendency of the graft component to kink in a single site is minimized and the resultant flexing is observed to take place in a collection of smaller non-kinking bends located among the tie points to the stent or the stent's filament.

A further variation of the inventive includes stent-grafts which are have open areas to allow access between the inner lumen and outer surface through the stent structure.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A, 1B, 1C, 1D, and 1E are plan views of an unrolled stent form making up the helical variation of the invention.

Figure 2 is a side view of the inventive helical stent.

Figure 3 is a close-up of a portion of the inventive helical stent shown in Figure 2.

Figure 4 is an abstracted portion of an inventive helical stent and shows the result of torsion on a portion of that stent.

Figure 5 is a side view of the inventive helical stent showing a variation having flared ends.

Figures 6, 7, and 8 show plan views of an unrolled helical stent produced from flat stock.

Figure 9 shows a quarter view of the rolled stent using the flat stock pattern shown in Figure 7.

Figure 10 shows a device for winding and heat treating a stent made according to the invention.

Figures 11 and 12 are close-ups of a portion of the inventive stent-graft showing multiple distributed attachment points between the stent and the graft.

Figure 13 shows a front quarter view of a stent graft of the type shown in Figures 11 and 12.

Figure 14 is a plan view of an unrolled stent form making up the ring variation of the inventive stent.

Figure 15 is a quarter view of a generic ring variation of the stent making up the invention.

Figure 16 is an end view and shows the placement of the inventive ring stent the bending of certain portions after placement.

Figure 17 is a cutaway close-up of the inventive ring stent shown in Figure 16.

Figure 18 is an abstracted portion of an inventive ring stent and shows the concept of causing a torsion on a portion of the stent.

Figure 19 shows a plan view of an unrolled stent produced from wire.

Figure 20 shows a plan view of an unrolled isolated ring making up a stent according to the invention.

Figure 21 shows a quarter view of the rolled isolated ring of Figure 20.

Figure 22 shows a plan view of multiple unrolled isolated rings suitable for making up a stent according to the invention.

Figures 23, 24, and 25 show plan views of variations of unrolled ring stents made according to the invention.

Figures 26 and 27 show end view cutaways of stent-grafts made according to the invention.

Figure 28 shows the placement of a continuous graft on a stent graft covering the entrance to a side branch.

Figures 29, 30, 31, and 32 show side-views of stent-grafts with non-continuous graft surfaces.

Figures 33A, 33C, and 33E show procedures for folding the stent-grafts made according to the invention. Figures 33B, 33D, and 33F show the corresponding folded stent-grafts.

Figures 34A-34C show a schematic procedure for deploying the inventive stent-grafts using an external sleeve.

Figures 35A and 36A show front quarter views of folded stents or stent-grafts held in that folded position by a tether wire. Figures 35B, 35C, 36B, and 36C show end views of the folded stent and of the open stent shown respectively in Figures 35A and 36A.

Figures 37A-37C show a schematic procedure for deploying the inventive stent-grafts (as shown in Figures 35A-35C and 36A-36C) using a tether wire.

Figure 38 shows a close-up view of a stent fold line using a preferred sack knot in the slip line.

Figures 39 and 40 show front quarter views of folded stents or stent-grafts held in that folded position by a tether wire using a sack knot.

DESCRIPTION OF THE INVENTION

As was noted above, this invention is variously an expandable stent, a stent-graft, and a fiber reinforced stent-graft. The stent-graft may be a combination of the following: a thin-walled tube (or graft) generally coaxial with the stent and the expandable stent structure. The tubular graft may comprise a porous polymeric tube, e.g., of an expanded PTFE, having a collagenous material embedded in te pores of the tube. The graft material may optionally contain fibrous reinforcement material. The stent and the optional reinforcing fibers may be imbedded in the wall of the thin-walled tube. The expandable stent structure is a generally cylindrical body produced either of a helically placed (wound or otherwise preformed) torsion member having an undulating or serpentine shape or a series of axially spaced rings comprising those torsion

members. When the undulating torsion member is formed into the cylinder, the undulations may be aligned so that they are "in phase" with each other. The undulations are desirably linked, typically with a flexible linkage of a suitable metallic or polymeric material, to maintain the phased relationship of the undulations during compression and deployment and during bending of the stent. These stent configurations are exceptionally kink-resistant and flexible, particularly when flexed along the longitudinal axis of the stent.

When the stent is used in a reinforced stent-graft, that is to say: the stent is included into a thin-walled tube having reinforcing fibers, the fibers may be formed into a network, such as a tubular mesh. The stent-graft may be delivered percutaneously through the vasculature after having been folded to a reduced diameter. Once reaching the intended delivery site, it is expanded to form a lining on the vessel wall.

Central to one variation of the invention is the distributed attachment of the stent component to the graft component via, e.g., the bonding of the graft to the filament which may used to maintain the stent in its tubular shape or via bonding to other loops, eyelets, or fasteners associated with or adhering to the stent component to allow the stent to move locally with respect to the graft and maintain the open structure of the graft lumen.

A further variation of the inventive includes stent-grafts which are have open areas to allow access between the inner lumen and outer surface through the stent structure.

Methods of delivering the various devices using a percutaneous catheter either with or without expansion aids are also an aspect of the invention.

Stent Component

The materials typically used for vascular grafts, e.g., synthetic polymers or fabrics or collagen, usually do not have the stiffness or strength alone both to stay open against the radial inward loads found in those vessels and to prevent their slippage from the chosen deployment site. In order to provide the strength required, a radially rigid stent structure may be incorporated into the stent-graft. Our stent is constructed of a reasonably high strength material, i.e., one which is resistant to plastic deformation when stressed. The structure is typically from one of three sources:

1.) a wire form in which a wire is first formed into an undulating shape and the resulting undulating shape is helically wound to form a cylinder,

2.) an appropriate shape is formed from a flat stock and wound into a cylinder, and

3.) a length of tubing is formed into an appropriate shape.

These stent structures are typically oriented coaxially with the tubular graft component. The stent structures may be placed on the outer surface or the inner surface of the tubular member although the stent may be imbedded in the graft tubing wall for ease of integration with the tubing and to prevent the stent's exposure to bodily fluids, such as blood. It is desired that the stent structure have the strength and flexibility to tack the

graft tubing firmly and conformally against the vessel wall. In order to minimize the wall thickness of the stent-graft, the stent material should have a high strength-to-volume ratio. The designs do not suffer from a tendency to twist (or helically unwind) or to shorten as the stent is deployed. As will be discussed below, materials suitable in these stents and meeting these criteria include various metals and some polymers.

A stent or stent-graft, whether delivered percutaneously or via a body orifice must expand from the reduced diameter necessary for delivery to a larger deployed diameter. The diameters of these devices obviously vary with the size of the body lumen into which they are placed. For instance, the stents of this invention may range in size from 2.0mm in diameter (for vascular neurological applications) to 30mm in diameter (for placement in the aorta). A range of about 2.0mm to 6.5mm (perhaps to 10.0mm) is believed to be desirable. Typically, expansion ratios of 2:1 or more are required. These stents are capable of expansion ratios of up to 5:1 for larger diameter stents. Typical expansion ratios for use with the stents and stent-grafts of the invention typically are in the range of about 2:1 to about 4:1 although the invention is not so limited. The thickness of the stent materials obviously varies with the size (or diameter) of the stent and the ultimate required yield strength of the folded stent. These values are further dependent upon the selected materials of construction. Wire used in these variations are typically of stronger alloys, e.g., nitinol and stronger spring stainless steels, and have diameters of about 0.002 inches to 0.005 inches. For the larger stents, the appropriate diameter for the stent wire may be somewhat larger, e.g., 0.005 to 0.020 inches. For flat stock metallic stents,

thicknesses of about 0.002 inches to 0.005 inches is usually sufficient. For the larger stents, the appropriate thickness for the stent flat stock may be somewhat thicker, e.g., 0.005 to 0.020 inches.

The stent-graft is fabricated in the expanded configuration. In order to reduce its diameter for delivery the stent-graft would be folded along its length, similar to the way in which a PCTA balloon would be folded. It is desirable, when using super-elastic alloys which are also have temperature-memory characteristics, to reduce the diameter of the stent at a temperature below the transition-temperature of the alloys. Often the phase of the alloy at the lower temperature is somewhat more workable and easily formed. For instance, at nitinol martensitic temperatures, the alloy material provides minimal resistance to folding and tends to maintain the folded configuration. The temperature of deployment is desirably above the transition temperature to allow use of the super-elastic properties of the alloy.

Thus, a preferred method for folding the stent-graft (when super-elastic alloys are used) comprises the steps of chilling the stent-graft to the martensitic temperature of the alloy, folding the stent-graft to the desired reduced diameter configuration and constraining the stent-graft in that folded configuration. The device is then allowed to warm to the austenitic temperature of the alloy (e.g., when the austenitic temperature is at or below room temperature) or above. This warming can be done, for example, before or after it is packaged. In use, the folded stent-graft is delivered to the treatment site and the constraint removed so that it can return to its original configuration to serve its intended purpose.

Alternatively, heat from the body or another

source coupled to the alloy material can be used to trigger the shape memory of the material. In that case, the alloy is selected to have an austenitic temperature above room temperature. Heat from the body or another source is used to heat the alloy material to its austenitic temperature as the device is delivered to the selected site so that upon release of the constraint, the device returns to its original configuration.

Helical stents

As a generic explanation of the mechanical theory of the helical variation of the inventive stent, reference is made to Figures 1A, 1B, 1C, 1D, 1E, 2, 3, and 4. Figure 1A is a plan view of an isolated section of the inventive stent device and is intended both to identify a variation of the invention and to provide conventions for naming the components of the torsion member (100). Figure 1A shows, in plan view, an undulating torsion member (100) formed from a wire stock into a U-shape. A torsion pair (102) is made up of an end member (104) and two adjacent torsion lengths (106). Typically, then, each torsion length (106) will be a component to each of its adjacent torsion pairs (102). The U-shaped torsion pair (102) may be characterized by the fact that the adjacent torsion lengths are generally parallel to each other prior to formation into the stent.

Generically speaking, the stents of this invention use undulating torsion members which are "open" or "unconfined" at their apex or end member (104). By "open" or "unconfined" we mean that the apex or end member (104) does not have any means in that apex which would tend to inhibit the movement of the flexible linkage (discussed below) down between the arms or torsion lengths (106) of the torsion pair (102).

Figure 1B shows another variation of the invention having a sinusoidal shaped torsion member (108). In this variation, the adjacent torsion lengths (110) are not parallel and the wire forms an approximate sine shape before being formed into a cylinder.

Figure 1C shows a variation of the invention having an ovoid shaped torsion member (112). In this variation, the adjacent torsion lengths (114) are again not parallel. The wire forms an approximate open-ended oval with each torsion pair (116) before being formed into a cylinder.

Figure 1D shows another variation of the invention having a V-shaped torsion member (118). In this variation, the adjacent torsion lengths (120) form a relatively sharp angle at the torsion end (122) shape before being formed into a cylinder.

Figure 1E shows a variation of the invention in which adjacent torsion members on the stent (117) have differing amplitude. The peaks of the high amplitude torsion members (119) may be lined up "out of phase" or "peak to peak" with short amplitude (121) or high amplitude torsion members in the adjacent turn of the helix or may be positioned "in phase" similar to those discussed with regard to Figure 2 below.

The configurations shown in Figs 1A-1E are exceptionally kink-resistant and flexible when flexed along the longitudinal axis of the stent.

As ultimately deployed, a section of the torsion member found on one of Figures 1A - 1D would be helically wound about a form of an appropriate size so that the end members (e.g., 104 in Figure 1A) would be centered between the end members of the torsion member on an adjacent turn of the helix. This is said to be "in phase". "Out of phase" would be the instance in which the

adjacent members meet directly, i.e., end member-to-end member. In any event, once so aligned, the phasic relationship may be stabilized by weaving a flexible linkage through the end members from one turn of the helix to the next.

Figure 2 shows a side view of a typical stent (122) made according to this invention including the phased relationship of the helical turns of the stent and the flexible linkage (124). Figure 3 shows a close-up of the Figure 2 stent and depicts the phased relationship (within box A) and shows in detail a typical way in which the flexible linkage (124) is looped through the various end members (104) to maintain the phased relationship. It may be noted that the flexible linkage (124) is free to move away from the apex at the end members (104) without constraint.

The stent may be folded in some fashion (as will be discussed below) for deployment. During the step of folding, the stent undergoes a transformation. Figure 4 shows an isolated torsion pair (102). When the torsion pair (102) undergoes a flexing in the amount of $\alpha°$, the end member will flex some amount $\beta°$, torsion length (130) will undertake a twist of $\gamma°$, and torsion length (132) will undertake a twist opposite of that found in torsion length (130) in the amount of $\delta°$. The amounts of angular torsion found in the torsion lengths (130 and 132) will not necessarily be equal because the torsion lengths are not necessarily at the same angle to the longitudinal axis of the stent. Nevertheless, the sum of $\beta°+\gamma°+\delta°$ will equal $\alpha°$. When a value of $\alpha°$ is chosen, as by selection of the shape and size of the stent upon folding, the values of the other three angles ($\beta°,\gamma°,\delta°$) are chosen by virtue of selection of number of torsion pairs around the stent, size and physical characteristics

of the wire, and length of the torsion lengths (103 and 132). Each of the noted angles must not be so large as to exceed the values at which the chosen material of construction plastically deforms at the chosen value of $\alpha°$.

To further explain the invention: it should understood that the torsion pair (102) undergoes a significant of flexing as the stent is folded or compressed in some fashion. The flexing provides a twist to the torsion lengths (103 and 132), a significant portion of which is generally parallel to the longitudinal axis of the stent. It is this significant imposed longitudinal torsion which forms an important concept of the inventive stent.

As noted elsewhere, in one very desirable variation of the inventive stent, as deployed in Figures 2 and 3, the stent is folded longitudinally and is delivered through the lumen of the catheter in such a way that it is self-restoring once it has been introduced to the selected body lumen site. This stated desire is not to rule out the use of the inventive stent or stent-graft with a balloon or expander or other shape-restoring tool if so desired, but the design of the stent is meant to eliminate the need for (or, at least to minimize the need for) such expanding tools.

With that preliminary background in place, it should be apparent that a simple tube of metal will undergo plastic deformation when sufficient force is applied radially to the outside of the tube. The amount of force needed to cause that plastic deformation will depend on a wide variety of factors, e.g., the type of metal utilized in the tube, the width of the tube, the circumference of the tube, the thickness of the material making up the band, etc. The act of attempting to fold a

tube along its centered axis in such a way to allow it to pass through a lumen having the same or smaller diameter and yet maintain the axis of the folded stent parallel to the axis of the lumen invites plastic deformation in and of the stent.

The inventive helical stent uses concepts which can be thought of as widely distributing and storing the force necessary to fold the tubular stent into a configuration which will fit through a diameter smaller than its relaxed outside diameter without inducing plastic deformation of the constituent metal or plastic and yet allowing those distributed forces to expand the stent upon deployment.

Once the concept of distributing the folding or compression stresses both into a bending component (as typified by angle $\beta°$ in Figure 4) and to twisting components (as typified by angle $\gamma°$ and $\delta°$ in Figure 4), and determining the overall size of a desired stent, determination of the optimum materials as well as the sizes of the various integral components making up the stent becomes straightforward. Specifically, the diameter and length of torsion lengths (130 and 132) and end sector (104), the number of torsion pairs (102) around the stent may then be determined.

Figure 5 shows, in side view, a variation of the inventive stent (140) made from wire having flares (142) at one or both ends. The flaring provides a secure anchoring of the stent or stent-graft (140) against the vessel wall. This prevents the implant from migrating downstream. In addition, the flaring provides a tight seal against the vessel so that the blood is channelled through the lumen rather than outside the graft. The undulating structure may vary in spacing to allow the helix turns to maintain its phased relationship between

turns of the helix and to conform to the discussion just above. A flexible linkage between the contiguous helical turns may also be applied to at least a portion of the helices.

The helical stent structure may also be made by forming a desired structural pattern out of a flat sheet. The sheet may then be rolled to form a tube. Figures 6, 7, and 8 show plan views of torsion members (respectively 200, 202, and 204) which may be then rolled about an axis (206) to form a cylinder. As is shown in Figure 9, the end caps (208) may be aligned so that they are "out of phase". The flexible linkage (210) is then included to preserve the diameter of the stent.

The stent shown in Figure 9 may be machined from tubing. If the chosen material in nitinol, careful control of temperature during the machining step may be had by EDM (electro-discharge-machining), laser cutting, chemical machining, or high pressure water cutting.

It should be clear that a variety of materials variously metallic, super elastic alloys, and preferably nitinol, are suitable for use in these stents. Primary requirements of the materials are that they be suitably springy even when fashioned into very thin sheets or small diameter wires. Various stainless steels which have been physically, chemically, and otherwise treated to produce high springiness are suitable as are other metal alloys such as cobalt chrome alloys (e.g., ELGILOY), platinum/tungsten alloys, and especially the nickel-titanium alloys generically known as "nitinol".

Nitinol is especially preferred because of its "super-elastic" or "pseudo-elastic" shape recovery properties, i.e., the ability to withstand a significant amount of bending and flexing and yet return to its original form without deformation. These metals are

characterized by their ability to be transformed from an austenitic crystal structure to a stress-induced martensitic structure at certain temperatures, and to return elastically to the austenitic shape when the stress is released. These alternating crystalline structures provide the alloy with its super-elastic properties. These alloys are well known but are described in U.S. Pat. Nos. 3,174,851, 3,351,463, and 3,753,700. Typically, nitinol will be nominally 50.6% (±0.2%) Ni with the remainder Ti. Commercially available nitinol materials usually will be sequentially mixed, cast, formed, and separately cold-worked to 30-40%, annealed, and stretched. Nominal ultimate yield strength values for commercial nitinol are in the range of 30 psi and for Young's modulus are about 700 kBar.

The '700 patent describes an alloy containing a higher iron content and consequently has a higher modulus than the Ni-Ti alloys. Nitinol is further suitable because it has a relatively high strength to volume ratio. This allows the torsion members to be shorter than for less elastic metals. The flexibility of the stent-graft is largely dictated by the length of the torsion member components in the stent structural component. The shorter the pitch of the device, the more flexible the stent-graft structure can be made. Materials other than nitinol are suitable. Spring tempered stainless steels and cobalt-chromium alloys such as ELGILOY are also suitable as are a wide variety of other known "super-elastic" alloys.

Although nitinol is preferred in this service because of its physical properties and its significant history in implantable medical devices, we also consider it also to be suitable for use as a stent because of its overall suitability with magnetic resonance imaging (MRI)

technology. Many other alloys, particularly those based on iron, are an anathema to the practice of MRI causing exceptionally poor images in the region of the alloy implant. Nitinol does not cause such problems.

Other materials suitable as the stent include certain polymeric materials, particularly engineering plastics such as thermotropic liquid crystal polymers ("LCP's"). These polymers are high molecular weight materials which can exist in a so-called "liquid crystalline state" where the material has some of the properties of a liquid (in that it can flow) but retains the long range molecular order of a crystal. The term "thermotropic" refers to the class of LCP's which are formed by temperature adjustment. LCP's may be prepared from monomers such as p,p'-dihydroxy-polynuclear-aromatics or dicarboxy-polynuclear-aromatics. The LCP's are easily formed and retain the necessary interpolymer attraction at room temperature to act as high strength plastic artifacts as are needed as a foldable stent. They are particularly suitable when augmented or filled with fibers such as those of the metals or alloys discussed below. It is to be noted that the fibers need not be linear but may have some preforming such as corrugations which add to the physical torsion enhancing abilities of the composite.

Figure 10 shows a method for producing a stent of the configuration shown in Figure 9. It may be used, of course, for producing a variety of other configurations shown herein. In this procedure, a preformed strip (211) (preferably nitinol) is rolled onto a mandrel (213) having a channel defined by a thread (215). The pitch of the strip (211) is selected using the criteria discussed above. The pitch angle (215) shown is about 20° but is not critical to the operation

of the invention. Once the strip (211) is wound onto the mandrel (213) and the assembly is introduced into the outer sleeve (217), the strip (now in the shape of the stent) may then be annealed (or at least "heat set") to assist in maintaining the resulting stent in a useful shape. For use in stents of the sizes mentioned elsewhere, we have found that nitinol devices may be heat treated for five minutes or less at temperatures of 500°C without significant lessening of the superelastic properties. Said another way, heating super-elastic alloys must carried out with some care so as not to destroy or significantly lessen the super-elastic properties.

The flexible linkage between adjacent turns of the helix (124 in Figs. 2 and 3) may be of any appropriate filamentary material which is blood compatible or biocompatible and sufficiently flexible to allow the stent to flex and not deform the stent upon folding. Although the linkage may be a single or multiple strand wire (platinum, platinum/tungsten, gold, palladium, tantalum, stainless steel, etc.), much preferred is the use of polymeric biocompatible filaments. Synthetic polymers such as polyethylene, polypropylene, polyurethane, polyglycolic acid, polyesters, polyamides, their mixtures, blends, copolymers, mixtures, blends and copolymers are suitable; preferred of this class are polyesters such as polyethylene terephthalate including DACRON and MYLAR and polyaramids such as KEVLAR, polyfluorocarbons such as polytetrafluoroethylene with and without copolymerized hexafluoropropylene (TEFLON or GORETEX), and porous or nonporous polyurethanes. Natural materials or materials based on natural sources such as collagen are especially preferred is this service.

Figure 11 shows a magnified portion of a stent-graft (viewed from the outside of the stent-graft) incorporating a stent such as is shown in Figures 2 and 3 and depicts a method for distributively attaching the stent to the graft component. Specifically, end member or apex (104) is flanked by side lengths (106) and is looped therethrough by a filament (124). The graft component (134) is seen in the background. The filament (124) adheres to the graft (134) at the locations of contact (138) between the filament (124) and the graft component (134). It should be apparent that the apexes (104) are free to move in the direction shown by arrows (148) when the stent-graft is flexed. This shows the ability of the various apexes to move longitudinally with respect to each other and yet retain the graft component (134) reasonably snug against the inner surface of the stent and thereby prevent kinking of that graft component (134).

Figure 12 shows a close-up of a section of a stent-graft according to the invention that is similar to the stent-graft portion shown in Figure 11 but in which the stent is attached to the graft using loops (150) or eyelets on the stent. Again this shows a manner of distributively attaching the stent to the graft component (134). Again, end member or apex (104) is flanked by side lengths (106). Although no filament (124 in Figure 11) is shown in the variation in Figure 12, it is contemplated that the filament (124) may be used in conjunction with loops (150). The graft component (134) is seen in the background. These loops (150) may be of a material which adheres to the graft component (134) at the junctions shown at (152). It is also contemplated that the filament (124) may be of material which is either adherent to (such as a melt-miscible thermoplastic

polymer) or not adherent to (such as a metal or thermoset polymer) the graft component (134) when used with the loops (152).

The scope of materials for the filament (124), graft component (134), and loops (152) will be discussed in detail below.

The stent support structure may also be made by forming a desired structural pattern out of a flat sheet. The formed sheet may then be rolled to form a tube. As is shown in Figure 13, the end caps (162) may be aligned so that they are "out of phase". The flexible linkage (164) may then be included to preserve the diameter of the stent. The graft component (166) is shown on the inner surface of the stent. Loops may be used as was described above. The graft may be attached to the loops or filament in the manner discussed above.

Ring-based stents

For a general explanation of the mechanical theory of the ring-based variation of the inventive stent, reference is made to Figures 14 to 17. Figure 14 is a conceptual schematic of an isolated ring section of the inventive stent device and is intended only to identify and to provide conventions for naming the components of the ring. Figure 14 shows, in plan view, the layout of the various components of a ring as if they were either to be cut from a flat sheet and later rolled into tubular formation for use as a stent with welding or other suitable joining procedures taking place at the seam or (if constructed from tubing) the layout as if the tubing was cut open. The portion of the stent between tie members (300) is designated as a ring (302) or ring section. Tie members (300) serve to link one ring (302) to an adjacent ring (302). A torsion pair (304) is made

up of a cap member (306) and two adjacent torsion members (308). Typically, then, each torsion member (308) will be a component to each of its adjacent torsion pairs (304).

As ultimately deployed, a roll of the sheet found in Figure 14 would be entered into the body lumen. Typically, it would be folded in some fashion which will be discussed below. A front quarter perspective view of the rolled stent is shown in the Figure 15. Figure 16 shows an end view of the deployed device. In Figure 16, the wall of the body vessel (310) is shown with the end view of cap members (306). As is more clearly shown in Figure 17, the end of the cap members (306) are separated into three distinct areas: Two opposing sectors (312) and a center sector (314). This distinction is made because as a bending moment is applied along the end of that cap member (306), the majority of the flexing in that cap member takes place along center sector (314). The angle (α) between the opposing sectors (312) is a measure of that flexing.

Further to the understanding of the concept of the ring-based stent device is Figure 18. Figure 18 shows an abstracted section of the sheet found in Figure 17 in which two cap members (306) and a torsion member (308) are shown in isolation from the Figure 14 sheet. Figure 18 shows the concept of the torsional twist angle (τ) as it relates to the ring-based stent. For the purposes of discussion here, the angles (α) and (τ) are measured from the same reference, the ends of the cap members (306) and assumes that the two cap members (306) shown in Figure 18 each define a plane as they are flexed and the two planes so defined are parallel to each other.

This desirable variation of the inventive stent, as deployed in Figures 16 and 17, may be folded

longitudinally and delivered via a catheter or other delivery mechanism much in the same way the helical stent is delivered. This stent may also be used with a balloon or expander or other shape-restoring tool if so desired, but the design of the stent is meant to eliminate the need for (or, at least to minimize the need for) such expanding tools.

This variation of the inventive stent uses the same design concept described above, i.e., distribution of the force necessary to fold the tubular stent into a configuration which will fit through a diameter smaller than its relaxed outside diameter without inducing plastic deformation of the constituent metal. Here, the force is distributed into two components: a bending component in cap member (306) -- especially in center sector (314) -- and a twisting or torsional component in torsion members (308).

Once the concept of distributing the folding or compressing stresses both into a bending component (as typified by angle α in Figure 17) and to a twisting component (as typified by angle τ in Figure 18), and determining the overall size of a desired stent, determination of the optimum materials as well as the sizes of the various integral components making up the stent becomes somewhat straightforward. Specifically, the length, width, and thickness of torsion members (308), the dimensions of an end cap center sector (314), the thickness of the material, and the remainder may then be determined. Obviously critical to the invention is the selection of the length, width, and thickness of torsion members (308) and the dimensions of end cap center sector (314) so that the bending angle α and twisting angle τ do not exceed the plastic deformation value of the selected stent material.

The materials suitable for this variation of the stent are those discussed above.

This stent structure may also be made by forming nitinol wire into the desired configuration. Various segments may be joined by welding. The desired structural pattern may be machined out of a flat sheet of nitinol. The sheet may then be rolled and the opposing edges welded to form a tube. The stent may be machined from nitinol tubing.

Figure 19 shows a plan view of a variation of the inventive stent (316) in which wire forms the various sectors of the stent. Torsion members (318) and end caps (320) forming ring portion (322) is also shown. Wire used in these variations are typically of stronger alloys, e.g., nitinol and stronger spring stainless steels, and have diameters of about 0.002 inches to 0.005 inches. For the larger stents, the appropriate diameter for the stent wire may be somewhat larger, e.g., 0.005 to 0.020 inches. Adjacent ring portions (322) may be joined by tie members (324). Tie members (324) may be welded to the end caps (320) by, e.g., welding. It should be apparent that any of the designs shown for cut sheet may, as an alternative, be constructed from wire instead.

Figure 20 shows a plan view of a ring section (304) of one variation of the inventive stent produced from a sheet. In this instance the end caps (306) and torsion members (308) form a single ring section which may be rolled and welded into an isolated ring (326) such as shown in Figure 21. Because the material chosen for the stent shown in Figures 20 and 21 is a highly elastic material such as nitinol, the length (328) of the torsion section (308) need not be so long as the length (330) of the end caps (306). Figure 22 shows a collection of individual rings (326) of the type shown in Figures 20

and 21 as they would be positioned in a stent-graft but prior to the time they are welded end-to-end.

Figure 23 shows a variation of the stent having a ring section (332) similar in configuration to that shown in Figures 20, 21, and 22 but joined by tie members (334). Those tie members (334) extend from the inside of a torsion pair (338) to the outside of a torsion pair (340) in the adjacent ring section. The tie members (334) experience no twisting because of their placement in the middle of end cap (342). The tie members may be offset on the end cap, if so desired, to allow the tie members to accept some of the twisting duty.

Figure 24 shows a plan view of a variation of the inventive stent in which the number of torsion members (344) in a selected ring member (346) is significantly higher then the number of torsion members found in the variations discussed in relation to Figures 20, 21, 22, and 23. This added number of torsion members may be due to a variety of reasons. For instance, the material of construction may have a significantly lower tolerance for twisting than the materials in those prior Figures. Adding more torsion bars lessens the load carried on each of the several bars. Alternatively, for the same material,the stent may need be folded to a smaller diameter for deployment than those earlier variations.

Figure 25 shows a variation of the invention in which the end caps (346) are bound by a long torsion member (348) and two short torsion members (350). This torsion set (352) is in turn separated from the adjacent torsion set (352) by a bridge member (354) which shores the bending load of the stent when the stent is rolled and the ends (356) joined by, e.g., welding. The torsion members (350) have a greater width than that of the long

torsion member (348) so to balance the load around the ring during deformation and thereby to prevent the bridge members from becoming askew and out of the ring plane.

Although it has been made quite clear that the stents and stent-grafts of this invention do not longitudinally expand as they are deployed, we have found it desirable in some instances to overlap the rings -- a single circumference would cross two or more rings -- to provide relief from kinking of the stent-graft. This is also particularly useful at the ends of the stent where additional strength is sometimes needed for securing the stent in place. Obviously to allow the rings to overlap without building thickness, the spacing and size of the end caps and torsion members must be tailored to intermesh without contact.

Tubular Graft Component

The tubular graft component or member of the stent-graft may be made up of any material which is suitable for use as a graft in the chosen body lumen. Many graft materials are known, particularly known are vascular graft materials. For instance, natural material may be introduced onto the inner surface of the stent and fastened into place. Synthetic polymers such as polyethylene, polypropylene, polyurethane, polyglycolic acid, polyesters, polyamides, their mixtures, blends, copolymers, mixtures, blends and copolymers are suitable; preferred of this class are polyesters such as polyethylene terephthalate including DACRON and MYLAR and polyaramids such as KEVLAR, polyfluorocarbons such as polytetrafluoroethylene with and without copolymerized hexafluoropropylene (TEFLON or GORETEX), and porous or nonporous polyurethanes.

Especially preferred in this invention are the expanded fluorocarbon polymers (especially PTFE) materials described in British. Pat. Nos. 1,355,373, 1,506,432, or 1,506,432 or in U.S. Pat. Nos. 3,953,566, 4,187,390, or 5,276,276, the entirety of which are incorporated by reference.

Included in the class of preferred expanded fluoropolymers are polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), copolymers of tetrafluoroethylene (TFE) and per fluoro(propyl vinyl ether) (PFA), homopolymers of polychlorotrifluoroethylene (PCTFE), and its copolymers with TFE, ethylene-chlorotrifluoroethylene (ECTFE), copolymers of ethylene-tetrafluoroethylene (ETFE), polyvinylidene fluoride (PVDF), and polyvinyfluoride (PVF). Especially preferred, because of its widespread use in vascular prostheses, is expanded PTFE.

Highly preferred materials are certain collagen-based materials of COLLAGEN CORPORATION of Palo Alto, California. The graft may adhere to or partially encapsulate or be cast about the stent when appropriate materials such as castable polyurethane or collagen-based materials are employed. When the stent-graft is produced in such a way that the openings in the stent contain graft material (as by casting), then we refer to such a stent-graft as an "integral stent-graft".

One very desirable variation of the invention involves the combination of a porous polymeric tubing member of one of the materials mentioned elsewhere herein, but most preferably of the expanded polyfluorocarbon polymers mentioned above, and a collagenous material imbedded into those pores. Specifically, the most preferred polymer is an expanded PTFE having an internodal distance of between 45 and 120

microns, more preferably between 60 and 90 microns. The preferred collagen material is that described below. This combination allows the polymeric tubing to provide structural reinforcement both for the overall stent and for the embedded collagen. The collagenous material still provides the benefits of endothelization mentioned elsewhere. The thickness of the graft need not be greater than the thickness of the polymeric tubing by itself, although it may be. The combination of synthetic polymeric tubing and collagenous material provides enhanced adhesion between the collagenous material and the stent and resistance to radial dimension changes (e.g., ballooning) which may be a problem when collagen is used alone.

A highly preferred collagen-based material is described in U.S. Pat. No. 5,162,430, to Rhee et al, the entirety of which is incorporated by notice, or as described below. Collagen is easily formed into thin-walled tubes which are limp, compliant, flexible, uniform, and have smooth surfaces. The tubing walls may have a hydrated thickness of 0.001 to 0.020 inches (or to 0.100 inches in some cases) for efficacy. Other thicknesses may be used if specific goals are to be achieved. In a stent-graft, the collagen tube acts as an intravascular blood conduit to line the interior surface of the blood vessel. It isolates the lined segment of the vessel from direct contact with blood flow, tacks any tears or dissections, helps reinforce the vessel wall to protect against or isolate aneurysms, and provides a smooth, relatively thin, conformal surface for the blood flow. Of most importance (at least from the perspective of the most preferred aspects of our invention), specific collagenous materials, such as the collagen-hydrophilic polymer conjugate described in U.S. Pat. No. 5,162,430

and as described below, are very desirable as the tubular component in this stent-graft in that they form non-thrombogenic surfaces which will support the growth of endothelium.

The preferred collagen composition used in this invention is a pharmaceutically acceptable non-immunogenic composition formed by covalently binding atelopeptide collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. Any type of collagen may be used including extracted and purified collagen including atelopeptide collagen which can be type I, type II or type III collagen. The collagen may be extracted from various sources such as bovine hide and human placenta and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The compositions may incorporate other components such as biologically active materials. The collagen-polymer conjugates generally contain large amounts of water when formed. The extruded materials may be dehydrated, resulting in a reasonably flexible material which can be readily stored.

The term "collagen" as used herein refers to all forms of collagen, including those which have been extracted, processed or otherwise modified. Preferred collagens are non-immunogenic and, if extracted from animals, are treated to remove the immunogenic telopeptide regions ("atelopeptide collagen"), are soluble, and may be in the fibrillar or non-fibrillar form. Type I collagen is best suited to most applications involving bone or cartilage repair. However, other forms of collagen are also useful in the

practice of the invention, and are not excluded from consideration here. Collagen crosslinked using heat, radiation, or chemical agents such as glutaraldehyde may be conjugated with polymers as described herein to form particularly rigid compositions. Collagen crosslinked using glutaraldehyde or other (nonpolymer) linking agents is referred to herein as "GAX", while collagen crosslinked using heat and/or radiation is termed "HRX." Collagen used in connection with the preferred embodiments of the invention is in a pharmaceutically pure form such that it can be incorporated into a body, human or otherwise, for the intended purpose.

The term "synthetic hydrophilic polymer" as used herein refers to a synthetic polymer having an average molecular weight and composition which renders the polymer essentially water-soluble. Preferred polymers are highly pure or are purified to a highly pure state such that the polymer is, or is treated to become, pharmaceutically pure. Most hydrophilic polymers can be rendered water-soluble by incorporating a sufficient number of oxygen (or, less frequently, nitrogen) atoms available for forming hydrogen bonds in aqueous solutions. Preferred polymers are hydrophilic but not soluble. Preferred hydrophilic polymers used herein include polyethylene glycol, polyoxyethylene, polymethylene glycol, polytrimethylene glycols, polyvinylpyrrolidones, and derivatives thereof. The polymers can be linear or multiply branched and will not be substantially crosslinked. Other suitable polymers include polyoxyethylene-polyoxypropylene block polymers and copolymers. Polyoxyethylene-polyoxypropylene block polymers having an ethylene diamine nucleus (and thus having four ends) are also available and may be used in the practice of the invention. Naturally occurring

and/or biologically active polymers such as proteins, starch, cellulose, heparin, and the like are not generally desirable in this definition although they may be used. All suitable polymers will be non-toxic, non-inflammatory and non-immunogenic when used to form the desired composition, and will preferably be essentially non-degradable <u>in vivo</u> over a period of at least several months. The hydrophilic polymer may increase the hydrophilicity of the collagen, but does not render it water-soluble. Presently preferred hydrophilic polymers are mono-, di-, and multi-functional polyethylene glycols (PEG). Monofunctional PEG has only one reactive hydroxy group, while difunctional PEG has reactive groups at each end. Monofunctional PEG preferably has a weight average molecular weight between about 100 and about 15,000, more preferably between about 200 and about 8,000, and most preferably about 4,000. Difunctional PEG preferably has a molecular weight of about 400 to about 40,000, more preferably about 3,000 to about 10,000. Multi-functional PEG preferably has a molecular weight between about 3,000 and 100,000.

PEG can be rendered monofunctional by forming an alkylene ether at one end. The alkylene ether may be any suitable alkoxy radical having 1-6 carbon atoms, for example, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, hexyloxy, and the like. Methoxy is presently preferred. Difunctional PEG is provided by allowing a reactive hydroxy group at each end of the linear molecule. The reactive groups are preferably at the ends of the polymer, but may be provided along the length thereof.

The term "chemically conjugated" as used herein means attached through a covalent chemical bond. In the practice of the invention, a synthetic hydrophilic polymer and collagen may be chemically conjugated by

using a linking radical, so that the polymer and collagen are each bound to the radical, but not directly to each other. The term "collagen-polymer" refers to collagen chemically conjugated to a synthetic hydrophilic polymer, within the meaning of this invention. Thus, "collagen-PEG" (or "PEG-collagen) denotes a composition within the most preferred aspect of the invention wherein collagen is chemically conjugated to PEG. "Collagen-dPEG" refers to collagen chemically conjugated to difunctional PEG, wherein the collagen molecules are typically crosslinked. "Crosslinked collagen" refers to collagen in which collagen molecules are linked by covalent bonds with polyfunctional (including difunctional) polymers. Terms such as "GAX-dPEG" and "HRX-dPEG" indicate collagen crosslinked by both a difunctional hydrophilic polymer and a crosslinking agent such as glutaraldehyde or heat. The polymer may be "chemically conjugated" to the collagen by means of a number of different types of chemical linkages. For example, the conjugation can be via an ester or urethane linkage, but is more preferably by means of an ether linkage. An ether linkage is preferred in that it can be formed without the use of toxic chemicals and is not readily susceptible to hydrolysis in vivo.

Those of ordinary skill in the art will appreciate that synthetic polymers such as polyethylene glycol cannot be prepared practically to have exact molecular weights, and that the term "molecular weight" as used herein refers to the weight average molecular weight of a number of molecules in any given sample, as commonly used in the art. Thus, a sample of PEG 2,000 might contain a statistical mixture of polymer molecules ranging in weight from, for example, 1,500 to 2,500 daltons with one molecule differing slightly from the

next over a range. Specification of a range of molecular weight indicates that the average molecular weight may be any value between the limits specified, and may include molecules outside those limits. Thus, a molecular weight range of about 800 to about 20,000 indicates an average molecular weight of at least about 800, ranging up to about 20 kDa.

The term "available lysine residue" as used herein refers to lysine side chains exposed on the outer surface of collagen molecules, which are positioned in a manner to allow reaction with activated PEG. The number of available lysine residues may be determined by reaction with sodium 2,4,6-trinitrobenzenesulfonate (TNBS).

The term "growth factor" is used to describe biologically active molecules and active peptides (which may be naturally occurring or synthetic) which aid in healing or regrowth of normal tissue. The function of growth factors is two-fold: 1) they can incite local cells to produce new collagen or tissue, or 2) they can attract cells to the site in need of correction. As such, growth factors may serve to encourage "biological anchoring" of the collagen graft implant within the host tissue. As previously described, the growth factors may either be admixed with the collagen-polymer conjugate or chemically coupled to the conjugate. For example, one may incorporate growth factors such as epidermal growth factor (EGF), transforming growth factor (TGF) alpha, TGF_{β} (including any combination of TGF_{β}s), $TGF_{\beta 1}$, $TGF_{\beta 2}$, platelet derived growth factor (PDGF-AA, PDGF-AB, PDGF-BB), acidic fibroblast growth factor (FGF), basic FGF, connective tissue activating peptides (CTAP), β-thromboglobulin, insulin-like growth factors, erythropoietin (EPO), nerve growth factor (NGF), bone morphogenic protein (BMP), osteogenic factors, and the like. Incor-

poration of growth factors can facilitate regrowth when the tubes are used in the treatment of defective or damaged channels. Furthermore, one may chemically link the growth factors to the collagen-polymer composition by employing a suitable amount of multi-functional polymer molecules during synthesis. The growth factors may then be attached to the free polymer ends by the same method used to attach PEG to collagen, or by any other suitable method. By tethering growth factors to the outer and/or inner surface of the graft material, the amount of grafts needed to carry out effective treatment is substantially reduced. Tubes which incorporate growth factors may provide effective controlled-release drug delivery. By varying the chemical linkage between the collagen and the synthetic polymer, it is possible to vary the effect with respect to the release of the biologic. For example, when an "ester" linkage is used, the linkage is more easily broken under physiological conditions, allowing for sustained release of the growth factor from the matrix. However, when an "ether" linkage is used, the bonds are not easily broken and the growth factor will remain in place for longer periods of time with its active sites exposed providing a biological effect on the natural substrate for the active site of the protein. It is possible to include a mixture of conjugates with different linkages so as to obtain variations in the effect with respect to the release of the biologic, e.g., the sustained release effect can be modified to obtain the desired rate of release.

The terms "effective amount" or "amount effective to treat" refer to the amount of composition required in order to obtain the effect desired. Thus, a "tissue growth-promoting amount" of a composition containing a growth factor refers to the amount of growth

factor needed in order to stimulate tissue growth to a detectable degree. Tissue, in this context, includes connective tissue, bone, cartilage, epidermis and dermis, blood, and other tissues with particular emphasis on tissues which form channels such as veins, arteries, intestines and the like. The actual amount which is determined to be an effective amount will vary depending on factors such as the size, condition, sex, and age of the patient, the type of tissue or channel, the effect desired and type of growth factor, and can be more readily determined by the caregiver.

The term "sufficient amount" as used herein is applied to the amount of carrier used in combination with the collagen-polymer conjugates used in forming the tubes of the invention. A sufficient amount is that amount which, when mixed with the conjugate, renders it in the physical form desired, for example, extrudable tubes, extrudable cylinders having any desired cross-section, and so forth. Extrudable formulations may include an amount of a carrier sufficient to render the composition smoothly extrudable without significant need to interrupt the extrusion process. The amount of the carrier can be varied and adjusted depending on the size and shape and thickness of the wall of the tube being extruded. Such adjustments will be apparent to those skilled in the art upon reading this disclosure.

Conjugates

To form the most desired collagen-conjugates used in the inventive stent-grafts, collagen must be chemically bound to a synthetic hydrophilic polymer. This can be carried out in a variety of ways. In accordance with the preferred method, the synthetic hydrophilic polymer is activated and then reacted with

the collagen. Alternatively, the hydroxyl or amino groups present on the collagen can be activated and the activated groups will react with the polymer to form the conjugate. In accordance with a less preferred method, a linking group with activated hydroxyl or amino groups thereon can be combined with the polymer and collagen in a manner so as to concurrently react with both the polymer and collagen forming the conjugate. Other methods of forming the conjugates will become apparent to those skilled in the art upon reading this disclosure. Since the conjugates of the invention are to be used in the human body it is important that all of the components, including the polymer, collagen, and linking group, if used form a conjugate that is unlikely to be rejected by the body. Accordingly, toxic and/or immunoreactive components are not preferred as starting materials. Some preferred starting materials and methods of forming conjugates are described further below.

Although different hydrophilic synthetic polymers can be used in connection with forming the conjugate, such polymers must be biocompatible, relatively insoluble, but hydrophilic and is preferably one or more forms of polyethylene glycol (PEG), due to its known biocompatibility. Various forms of PEG are extensively used in the modification of biologically active molecules because PEG can be formulated to have a wide range of solubilities and because it lacks toxicity, antigenicity, immunogenicity, and does not typically interfere with the enzymatic activities and/or conformations of peptides. Further, PEG is generally non-biodegradable and is easily excreted from most living organisms including humans.

The first step in forming the collagen-polymer conjugates generally involves the functionalization of

the PEG molecule. Various functionalized polyethylene glycols have been used effectively in fields such as protein modification (see Abuchowski et al., Enzymes as Drugs, John Wiley & Sons: New York, NY (1981) pp. 367-383; and Dreborg et al., Crit. Rev. Therap. Drug Carrier Syst. (1990) 6:315, both of which are incorporated herein by reference), peptide chemistry (see Mutter et al., The Peptides, Academic: New York, NY 2:285-332; and Zalipsky et al., Int. J. Peptide Protein Res. (1987) 30:740, both of which are incorporated herein by reference), and the synthesis of polymeric drugs (see Zalipsky et al., Eur. Polym. J. (1983) 19:1177; and Ouchi et al., J. Macromol. Sci. -Chem. (1987) A24:1011, both of which are incorporated herein by reference). Various types of conjugates formed by the binding of polyethylene glycol with specific pharmaceutically active proteins have been disclosed and found to have useful medical applications in part due to the stability of such conjugates with respect to proteolytic digestion, reduced immunogenicity and longer half-lives within living organisms.

One form of polyethylene glycol which has been found to be particularly useful is monomethoxy-polyethylene glycol (mPEG), which can be activated by the addition of a compound such as cyanuric chloride, then coupled to a protein (see Abuchowski et al., J. Biol. Chem. (1977) 252:3578, which is incorporated herein by reference). Although such methods of activating polyethylene glycol can be used in connection with the present invention, they are not particularly desirable in that the cyanuric chloride is relatively toxic and must be completely removed from any resulting product in order to provide a pharmaceutically acceptable composition.

Activated forms of PEG can be made from reactants which can be purchased commercially. One form

of activated PEG which has been found to be particularly useful in connection with the present invention is mPEG-succinate-N-hydroxysuccinimide ester (SS-PEG) (see Abuchowski et al., Cancer Biochem. Biphys. (1984) 7:175, which is incorporated herein by reference). Activated forms of PEG such as SS-PEG react with the proteins under relatively mild conditions and produce conjugates without destroying the specific biological activity and specificity of the protein attached to the PEG. However, when such activated PEGs are reacted with proteins, they react and form linkages by means of ester bonds. Although ester linkages can be used in connection with the present invention, they are not particularly preferred in that they undergo hydrolysis when subjected to physiological conditions over extended periods of time (see Dreborg et al., Crit. Rev. Therap. Drug Carrier Syst. (1990) 6:315; and Ulbrich et al., J. Makromol. Chem. (1986) 187:1131, both of which are incorporated herein by reference).

It is possible to link PEG to proteins via urethane linkages, thereby providing a more stable attachment which is more resistant to hydrolytic digestion than the ester linkages (see Zalipsky et al., Polymeric Drug and Drug Delivery Systems, Chapter 10, "Succinimidyl Carbonates of Polyethylene Glycol" (1991) incorporated herein by reference to disclose the chemistry involved in linking various forms of PEG to specific biologically active proteins). The stability of urethane linkages has been demonstrated under physiological conditions (see Veronese et al., Appl. Biochem. Biotechnol. (1985) 11:141; and Larwood et al., J. Labelled Compounds Radiopharm. (1984) 21:603, both of which are incorporated herein by reference). Another means of attaching the PEG to a protein can be by means

of a carbamate linkage (see Beauchamp et al., Anal. Biochem. (1983) 131:25; and Berger et al., Blood (1988) 71:1641, both of which are incorporated herein by reference). The carbamate linkage is created by the use of carbonyldiimidazole-activated PEG. Although such linkages have advantages, the reactions are relatively slow and may take 2 to 3 days to complete.

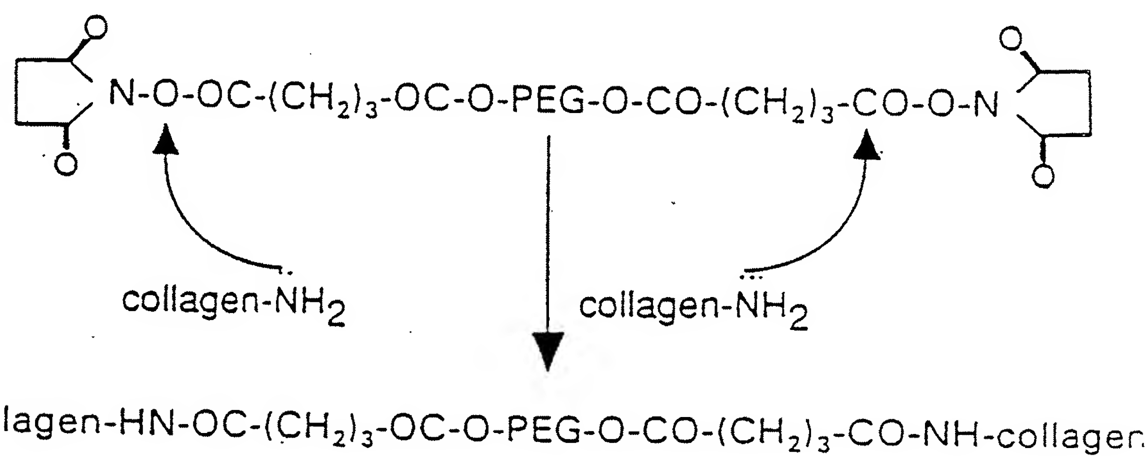
The various means of activating PEG described above and publications (all of which are incorporated herein by reference) cited in connection with the activation means are described in connection with linking the PEG to specific biologically active proteins and not collagen. However, the present invention now discloses that such activated PEG compounds can be used in connection with the formation of collagen-PEG conjugates. Such conjugates provide a range of improved characteristics and as such can be used to form the various compositions used in forming the tubes of the present invention. [Polymeric Drug and Drug Delivery Systems, Chapter 10, "Succinimidyl Carbonates of Polyethylene Glycol" (1991), incorporated herein by reference to disclose the chemistry involved in linking various forms of PEG to specific biologically active proteins.]

As indicated above, the conjugates used in forming the grafts may be prepared by covalently binding a variety of different types of synthetic hydrophilic polymers to collagen. However, because the final product or conjugate obtained must have a number of required characteristics such as being extrudable from a nozzle, biocompatible and non-immunogenic, it has been found useful to use polyethylene glycol as the synthetic hydrophilic polymer. The polyethylene glycol must be modified in order to provide activated groups on one or

preferably both ends of the molecule so that covalent binding can occur between the PEG and the collagen. Some specific functionalized forms of PEG are shown structurally below, as are the products obtained by reacting these functionalized forms of PEG with collagen.

The first functionalized PEG is difunctionalized PEG succinimidyl glutarate, referred to herein as (SG-PEG). The structural formula of this molecule and the reaction product obtained by reacting it with collagen is shown in Formula 1.

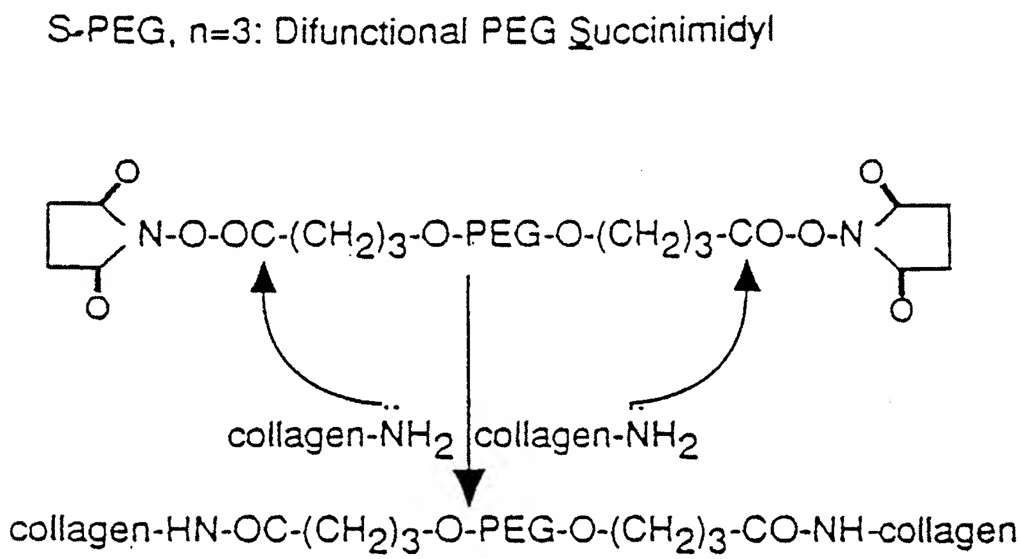
S-PEG: Difunctional PEG Succinimidyl Glutarate



FORMULA 1

Another difunctionally activated form of PEG is referred to as PEG succinimidyl (S-PEG). The structural formula for this compound and the reaction product obtained by reacting it with collagen is shown in Formula 2. In a general structural formula for the compound of Formula 2, the subscript 3 is replaced with an "n." In the embodiment shown in Formula 1, n=3, in

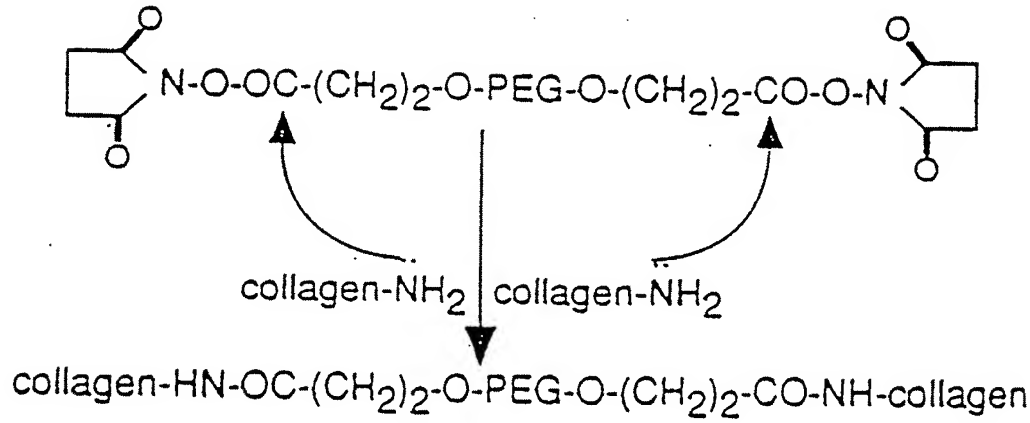
that there are three repeating CH_2 groups on each side of the PEG. The structure in Formula 2 results in a conjugate which includes an "ether" linkage which is not subject to hydrolysis. This is distinct from the first conjugate shown in Formula 1, wherein an ester linkage is provided. The ester linkage is subject to hydrolysis under physiological conditions.



FORMULA 2

Yet another derivatized form of polyethylene glycol, wherein n=2 is shown in Formula 3, as is the conjugate formed by reacting the derivatized PEG with collagen.

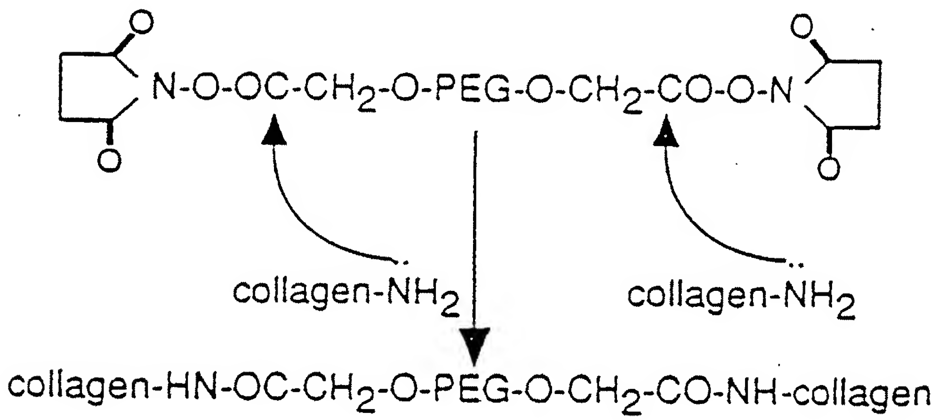
S-PEG, n=2: Difunctional PEG Succinimidyl



FORMULA 3

Another preferred embodiment of the invention similar to the compounds of Formula 2 and Formula 3, is provided when n=1. The structural formula and resulting conjugate are shown in Formula 4. It is noted that the conjugate includes both an ether and a peptide linkage. These linkages are stable under physiological conditions.

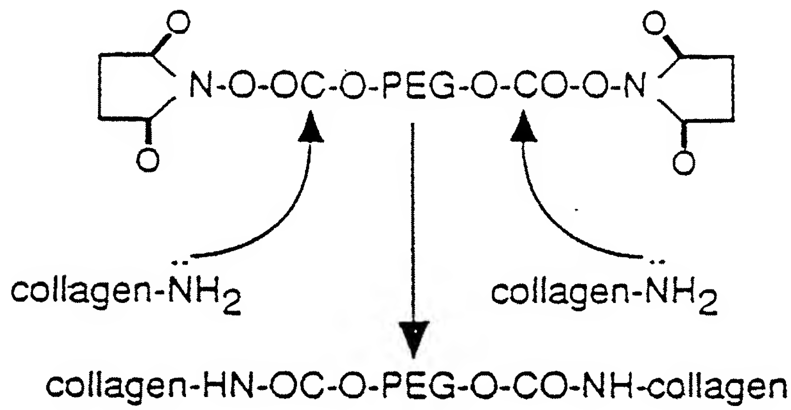
S-PEG, n=1: Difunctional PEG Succinimidyl



FORMULA 4

Yet another derivatized form of PEG is provided when n=0. The difunctionalized form is referred to as PEG succinimidyl carbonate (SC-PEG). The structural formula of this compound and the conjugate formed by reacting SC-PEG with collagen is shown in Formula 5. Although this conjugate includes a urethane linkage, the conjugate has been found not to have a high degree of stability under physiological conditions. The instability can be a desirable characteristic when the tubes are used in a situation where it is desirable that they dissolve over time.

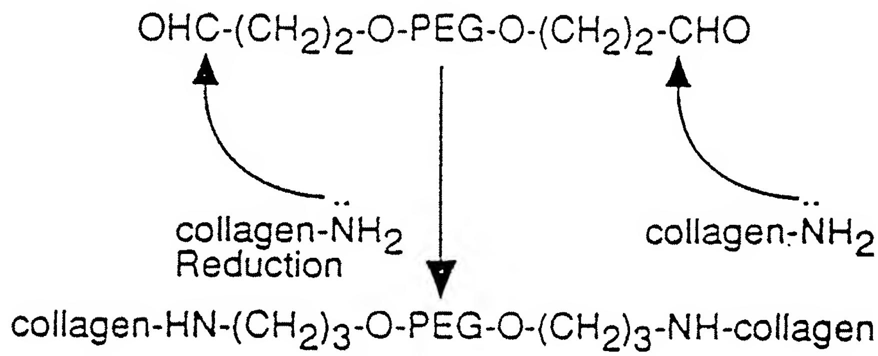
SC-PEG, n=0: Difunctional PEG Succinimidyl Carbonate



FORMULA 5

All of the derivatives depicted in Formulas 1-5 involve the inclusion of the succinimidyl group. However, different activating groups can be attached to one or both ends of the PEG. For example, the PEG can be derivatized to form difunctional PEG propionaldehyde (A-PEG), which is shown in Formula 6, as is the conjugate formed by the reaction of A-PEG with collagen.

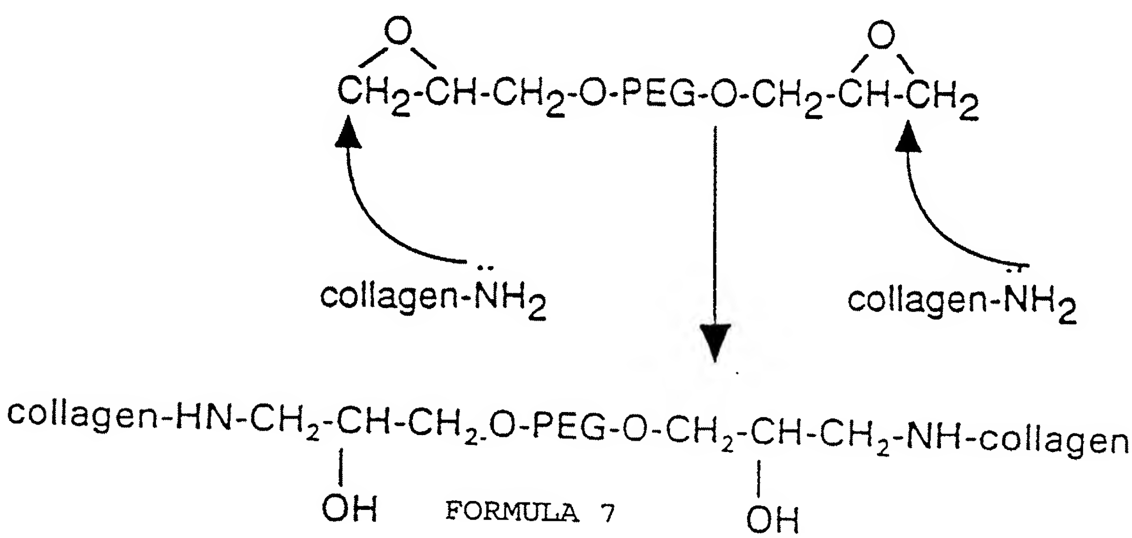
A-PEG: Difunctional PEG Propion Aldehyde



FORMULA 6

Yet another functionalized form of polyethylene glycol is difunctional PEG glycidyl ether (E-PEG), which is shown in Formula 7, as

E-PEG: Difunctional PEG Glycidyl Ether



FORMULA 7

The conjugates formed using the functionalized forms of PEG vary depending on the functionalized form of PEG which is used in the reaction. Furthermore, the final product can be varied with respect to its characteristics by changing the molecular weight of the PEG. In general, the stability of the conjugate is improved by eliminating any ester linkages between the PEG and the collagen and including ether and/or urethane linkages. These stable linkages are generally used to form tubes to replace or augment a channel as may be done with a stent-graft. When the grafts are used as a temporary repair unit for a damaged channel, it may be desirable to include the weaker ester linkages so that the linkages are gradually broken by hydrolysis under physiological conditions, breaking apart the tube as it may be replaced by host tissue, or as it degrades, and releasing a component held therein, such as a growth factor. By varying the chemical structure of the linkage, the rate of sustained release can be varied.

Suitable collagens include all types of pharmaceutically useful collagen, preferably types I, II and III. Collagens may be soluble (for example, commercially available Vitrogen® 100 collagen-in-solution), and may or may not have the telopeptide regions. Preferably, the collagen will be reconstituted fibrillar atelopeptide collagen, for example Zyderm® collagen implant (ZCI) or atelopeptide collagen in solution (CIS). Various forms of collagen are available commercially, or may be prepared by the processes described in, for example, U.S. Pat. Nos. 3,949,073; 4,488,911; 4,424,208; 4,582,640; 4,642,117; 4,557,764; and

4,689,399, all incorporated herein by reference. Fibrillar, atelopeptide, reconstituted collagen is preferred in order to form tubes used for the repair or augmentation of channels.

Compositions used in forming the invention comprise collagen chemically conjugated to a selected synthetic hydrophilic polymer or polymers. Collagen contains a number of available amino and hydroxy groups which may be used to bind the synthetic hydrophilic polymer. The polymer may be bound using a "linking group", as the native hydroxy or amino groups in collagen and in the polymer frequently require activation before they can be linked. For example, one may employ compounds such as dicarboxylic anhydrides (e.g., glutaric or succinic anhydride) to form a polymer derivative (e.g., succinate), which may then be activated by esterification with a convenient leaving group, for example, N-hydroxysuccinimide, N,N'-disuccinimidyl oxalate, N,N'-disuccinimidyl carbonate, and the like. See also Davis, U.S. Pat. No. 4,179,337 for additional linking groups. Presently preferred dicarboxylic anhydrides that are used to form polymer-glutarate compositions include glutaric anhydride, adipic anhydride, 1,8-naphthalene dicarboxylic anhydride, and 1,4,5,8-naphthalenetetracarboxylic dianhydride. The polymer thus activated is then allowed to react with the collagen, forming a collagen-polymer composition used to make the grafts.

In one highly desirable embodiment having ester linkages, a pharmaceutically pure form of monomethylpolyethylene glycol (mPEG) (mw 5,000) is reacted with glutaric anhydride (pure form) to create mPEG glutarate. The glutarate derivative is then reacted with N-hydroxysuccinimide to form a succinimidyl monomethylpolyethylene glycol glutarate. The succinimidyl ester (mPEG*,

denoting the activated PEG intermediate) is then capable of reacting with free amino groups present on collagen (lysine residues) to form a collagen-PEG conjugate wherein one end of the PEG molecule is free or nonbound. Other polymers may be substituted for the monomethyl PEG, as described above. Similarly, the coupling reaction may be carried out using any known method for derivatizing proteins and synthetic polymers. The number of available lysines conjugated may vary from a single residue to 100% of the lysines, preferably 10-50%, and more preferably 20-30%. The number of reactive lysine residues may be determined by standard methods, for example by reaction with TNBS.

The resulting product is a smooth, pliable, rubbery mass having a shiny appearance. It may be wetted, but is not water-soluble. It may be formulated as a suspension at any convenient concentration, preferably about 30-65 mg/mL, and may be extruded through a nozzle to form a tube. The consistency of the formulation may be adjusted by varying the amount of liquid used.

<u>Production of a Stent-Graft comprising collagen</u>

One method of constructing a collagen-containing stent-graft is to first construct the stent and then to mold or cast the collagen tubular component about the stent.

The stent structure and any fiber reinforcement may be molded into the wall of the collagen tube. A mold for such a structure desirably is a simple annular space between two cylinders having room in the annular space for placement of the stent and would have a longitudinal axis slightly longer than the length of the stent-graft to be produced. The stent and fiber tubing is centered in the annular space and then the remaining space filled

with collagen. If sPEG cross-linked collagen is used as the matrix material, the sPEG and collagen are mixed and introduced into the mold and allowed to cure. After curing, the mold is separated and the inventive fiber reinforced collagen tube with a stent structure produced.

Another method of producing a composite stent-graft is to attach a porous polymeric tubing to the stent in the manner mentioned elsewhere herein, e.g., by loop or attachment to the flexible linkage, and then to add the collagenous material to the pores in the tubing in the manner mentioned above.

Stent-Graft

The tubular component, whether collagen-based or not, may also be reinforced using a network of small diameter fibers. The fibers may be random, braided, knitted, or woven. The fibers may be imbedded in the tubular component, may be placed in a separate layer coaxial with the tubular component, or may be used in a combination of the two.

Figure 26 shows an end view, cross-section of the configuration in which the stent (360) forms the outermost layer, a fibrous layer (362) coaxial to and inside the stent (360), and the tubular component (364) of, e.g., collagen as the innermost layer.

Particularly desirable is the variation shown in Figure 27 in which the fibrous material is mixed with or imbedded into the tubular layer (366) and cast or injected around the stent (360). This fibrous material may extend for the length of the device or may be shorter. The fibers may be wound or placed in any reasonable orientation within the device. Alternatively, randomly oriented short segments of fibers may also be imbedded in the wall of the tubing. The

fiber may be any suitable fibrous blood-compatible material including polyesters such as DACRON, polyamides such as NYLON, KEVLAR, polyglycolic acids, polylactic acids, polyethylene, polypropylene, silk or other strong flexible fiber which are not detrimentally affected in the medical service in which this device is placed. Specifically, polypropylene and the like will not be dissolved in blood but polyglycolic acid will dissolve. Each are suitable but work in different ways.

In addition, one or more radio-opaque metallic fibers, such as gold, platinum, platinum-tungsten, palladium, platinum-iridium, rhodium, tantalum, or alloys or composites of these metals like may be incorporated into the multi-strand reinforcement network to allow fluoroscopic visualization of the device.

In the collagen-fiber composite tube, the fibers carry much of the hoop stress and other loadings imposed by the vessel. This relieves the loading on the collagen and significantly increases the burst strength and fatigue properties of the tube. In addition, this makes the tube more effective in hydraulically isolating the vessel and as a result prevents the formation or worsening of aneurysms. This would be particularly beneficial in thinned weakened vessel walls resulting from de-bulking interventions or from medial thinning that has been seen to accompany stent placement. Another benefit of the fiber reinforcement is the increase in resistance to radially inward loading, especially if the loading is very focussed. Finally, fiber reinforcement may also impart some longitudinal stiffness to the stent-graft. This allows the stent-graft to maintain its strength and prevent it from kinking or sagging into the lumen.

In some instances it is desirable to produce a stent-graft having a non-continuous graft member. For instance, Figure 28 shows a situation in which a stent - graft (370) having a continuous graft layer has been deployed in an artery over a side branch (372) thereby blocking perfusion to that branch (372). In some cases, a significant amount of tissue may be compromised as a result. Bare stents of the same configuration as the stent in stent-graft (370) would be adequate to allow flow of blood into that side branch (372). Figures 29, 30, and 31 depict combination stent-grafts which have non-continuous graft members. In Figure 29 is found a stent-graft (374) having two separate graft sections (376) with a bare stent section (378) in the center. The bare stent section (378) allows blood flow through the stent mesh for side branches as seen in Figure 28. A further variation is seen in Figure 30. The combination stent-graft (380) with a bare stent end (382) and a single end graft (384). Figure 31 shows still another variation of the combination stent-graft (386) in which two short stent sections (388) associated with a graft material are separated by a series of links (390). The central link section is sufficient to allow flow of blood (or other fluids) through that area.

Another variation in which the graft layer (392) is discontinuous over the stent (394) is shown in Figure 32. In this instance the discontinuity is formed through the presence of discrete holes (396) through the graft layer. When used in a blood vessel, the stent-graft with holes will allow endothelial cells on the outside of the vessel to grow onto the inside of the stent-graft. Conventional vascular grafts only allow endothelial cells in the vessel to grow on the inner or flowing surface to grow from the ends of the graft.

Deployment of the Invention

When a stent-graft having torsion members is folded, crushed, or otherwise collapsed, mechanical energy is stored as a twist in those torsion members. In this loaded state, the torsion members have a torque exerted about them and consequently have a tendency to untwist. Collectively, the torque exerted by the torsion members as folded down to a reduced diameter must be restrained from springing open. The stent typically has at least one torsion member per fold to take advantage of the invention. The stent-graft is folded along its longitudinal axis and restrained from springing open. The stent-graft is then deployed by removing the restraining mechanism, thus allowing the torsion members to spring open against the vessel wall.

The attending surgeon will choose a stent or stent-graft having an appropriate diameter. However, inventive devices of this type are typically selected having an expanded diameter of up to about 10% greater than the diameter of the lumen to be the site of the stent deployment.

Figure 33A shows a sequence of folding the tubular device (400) of this invention about a guidewire (402) into a loose C-shaped configuration. Figure 33B shows a front quarter view of the resulting folded stent or stent-graft.

Figure 33C shows a sequence of folding the device (400) of this invention about a guidewire (402) into a rolled configuration. Figure 33D shows a front quarter view of the resulting folded stent or stent-graft.

Figure 33E shows a sequence of folding the device (400) of this invention about a guidewire (402) into a triple lobed configuration. Figure 33F shows a

front quarter view of the resulting folded stent or stent-graft.

The stent-graft may be tracked through the vasculature (or other bodily lumen) to the intended deployment site and then unfolded against the vessel lumen. The graft tube component of the stent-graft is limp, flexible, and thus easy to fold. Folding of the stent structure in the manner discussed above allows it to return to a circular, open configuration.

Figures 34A-34C show one desired way to place the devices of the present invention and allow them to self-expand. Figure 34A shows a target site (406) having, e.g., a narrowed vessel lumen. A guidewire (408) having a guide tip (409) has been directed to the site using known techniques. The stent-graft (410) is mounted on tubing (412) inside outer sliding sheath (416) after having folded in the manner discussed above. The outer sliding sheath (416) binds the compressed stent-graft (410) in place until released.

Figure 34B shows placement of the stent-graft (410) at the selected site (406) by sliding the stent-graft (410) over the guidewire (408) all together with the guidewire tubing (412) and the outer sliding sheath (414). The stent-graft (410) is deployed by holding the guidewire tubing (412) in a stationary position while withdrawing the outer sliding sheath (414). The stent-graft (410) can be seen in Figure 34B as partially deployed.

Figure 34C shows the stent-graft (410) fully deployed after the guidewire tubing (412) and the outer sliding sheath (414) have been fully retracted.

Figures 35A-C, 36A-C, and 37A-C show an inventive variation of deploying a stent or stent-graft made according to this invention. These methods involve

the use of a control line or tether line (420) which maintains the stent or stent-graft in a folded configuration until release.

Figure 35A is a front-quarter view of the stent (422) or stent-graft which has been folded as shown in the Figures discussed above. The stent (422) is folded about guidewire (424) so that, when deployed, the guidewire (424) is within the stent (422). Central to the variation shown here is the tether wire (420) which is passed through loops (426) associated with the various helices as they wind about the stent (422). The loops (426) may be formed from the flexible link (124 in Figures 2 or 3) or may be simply an alternating weave through appropriate apexes of the undulating helix, e.g., (104 in Figure 3) or may be loops specifically installed for the purpose shown here. It should be clear that the tether wire (426) is so placed that when it is removed by sliding it axially along the stent (422) and out of the loops (426), that the stent (422) unfolds into a generally cylindrical shape within the body lumen.

Figure 35B shows an end-view of a folded stent (422) or stent-graft having a guidewire (424) within the inner surface of the stent (422) and with the tether wire (420) within the loops (426). The end view of the folded stent (422) shows it to be folded into a form which is generally C-shaped. When expanded by removal of the tether wire (420), the stent (422) in Figure 35B assumes the form shown in end view in Figure 35C. There may be seen the guidewire (424) within the lumen of the stent (422) and the loops (426) which were formerly in a generally linear relationship having a tether wire passing through them.

Figure 36A shows a folded stent (428) (or stent-graft) in front quarter view which is similar in

configuration to the stent (422) shown in Figure 35A except that the stent (428) is rolled somewhat tighter than the previously discussed stent. The guidewire (424) is also inside the stent (428) rather than outside of it. Loops (426) from generally opposing sides of the stent (428) are folded into an approximate line so that the tether wire may pass through the aligned loops (426). Figure 36B shows an end view of the stent (428), and in particular, emphasizes the tighter fold of the stent (428). When expanded by removal of the tether wire (420), the stent (428) in Figure 36B assumes the form shown in Figure 33C. In Figure 33C may be seen the guidewire (424) within the lumen of the stent (428) and the loops (426) which were formerly in a generally linear relationship having a tether wire passing through them.

Figures 37A-C show a schematic procedure for deploying the stent (430) (or stent-graft) using a percutaneous catheter assembly (432).

In Figure 37A may be seen a percutaneous catheter assembly (432) which has been inserted to a selected site (434) within a body lumen. The stent (430) is folded about the guidewire and guidewire tube (436) held axially in place prior to deployment by distal barrier (438) and proximal barrier (440). The distal barrier (438) and proximal barrier (440) typically are affixed to the guidewire tube (436). The tether wire (420) is shown extending through loops (426) proximally through the catheter assembly's (432) outer jacket (442) through to outside the body.

Figure 37B shows the removal of the tether wire (420) from a portion of the loops (426) to partially expand the stent (430) onto the selected site (434).

Figure 37C shows the final removal of the tether wire (420) from the loops (426) and the retraction

of the catheter assembly (432) from the interior of the stent (430). The stent (430) is shown as fully expanded.

Figure 38 shows a close-up of a stent fold line having the familiar herringbone pattern of the "sack knot" used to close the fold in the stent. This knot is the one used to hold, e.g., burlap sacks of feed grain closed prior to use and yet allow ease of opening when the sack is to be opened. In this variation, the slip line has a fixed end (520) and a release end (522). loops of the slip line pass through the eyelets (524) on the side of the stent fold associated with the fixed end (520) and are held in place by eyelets (526) on the side of the stent fold associated with the release end (522). The fixed end (520) is not typically tied to the stent so to allow removal of the slip line after deployment. The eyelets (524 and 526) are desirable but optional. The eyelets (524 and 526) may be wire or polymeric thread or the like tied to the stent structure at the edge of the stent fold. If so desired, the loops may be dispensed with and the slip line woven directly into the stent structure. The self-expanding stent may be deployed by pulling axially on release end (522) as shown by the arrow in the drawing.

Figures 39 and 40 show front quarter views of folded stents using the knot shown in Figure 38. Figure 39 shows the use of a single stent fold similar in configuration to those described above. As was shown in Figure 38, the fixed end (520) portion of the slip line is associated with a row of eyelets (524) which are tied or otherwise fixed to the stent. The release end (522) is associated with the other row of eyelets (526).

Figure 37 depicts the use of multiple stent folds each having a fixed end (520 & 530) and a release end (522 & 532) on their respective slip lines.

The variations of the invention shown in Figures 38-40 may be introduced in to the body using the procedures outlined above with relation to Figures 34-37.

Although we generally discuss the deployment of the stent or stent-graft using a catheter, often deployed percutaneously, it should be apparent that the procedure and the folded stent or stent-graft are not so limited. The folded stent or stent-graft may also be deployed through artificial or natural body openings with a sheath or endoscopic delivery device perhaps without a guidewire. Similarly, the stent or stent graft may be delivered manually during a surgical procedure.

Many alterations and modifications may be made by those of ordinary skill in the art without departing from the spirit and scope of the invention. The illustrated embodiments have been shown only for purposes of clarity and examples, and should not be taken as limiting the invention as defined by the following claims, which include all equivalents, whether now or later devised.

WE CLAIM AS OUR INVENTION:

1. A stent for introduction into a body lumen having: a generally cylindrical form with two ends, a passageway having a radius extending between those ends, and an axis extending along said passageway, said stent comprising:

at least one assembly comprising at least one torsion member, said torsion member being situated so that when said assembly is distorted, said torsion member is twisted.

2. The stent of claim 1 where the at least one assembly is a helically aligned torsion member defining said cylinder, said helically aligned torsion member having undulating elements having unconfining apexes.

3. The stent of claim 2 wherein said undulating elements are arranged so that said apexes are in an intercooperating phased relationship between adjacent helical turns.

4. The stent of claim 3 additionally comprising at least one flexible link passing through said undulating elements on adjacent helical turns.

5. The stent of claim 1 wherein said at least one torsion member is positioned so to cause the stent to be self-expanding upon release of the distortion.

6. The stent of claim 1 where the stent is formed of wire.

7. The stent of claim 2 where the torsion member comprises a material selected from stainless steels,

cobalt chromium alloys, platinum/tungsten alloys, and nickel-titanium alloys.

8. The stent of claim 7 where the torsion member comprises a superelastic alloy.

9. The stent of claim 8 where the torsion member comprises nitinol.

10. The stent of claim 2 where the torsion member comprises a sheet material.

11. The stent of claim 2 where the torsion member is produced from tubing.

12. The stent of claim 4 wherein the flexible link is a polymeric thread or wire.

13. The stent of claim 1 where the at least one assembly is at least one ring assembly extending circumferentially about said passageway, each said ring assembly containing at least one torsion member approximately parallel to said axis, said torsion member being situated so that when said ring assembly is distorted, said torsion member is twisted.

14. The stent of claim 13 comprising more than one ring assembly.

15. The stent of claim 14 where the ring assemblies are joined with tie members which are generally parallel to said axis.

16. The stent of claim 1 additionally comprising a tubular member coaxial with at least a portion of the passageway.

17. The stent of claim 16 where the tubular member comprises a material selected from polyethylene, polypropylene, polyglycolic acid, polyesters, polyamides, their mixtures, blends, copolymers, mixtures, blends and copolymers; polyesters, polyaramids, polyfluorocarbons, and porous or nonporous polyurethanes; and collagenous materials.

18. The stent of claim 16 where the tubular member comprises porous or non-porous polytetrafluoroethylene.

19. The stent of claim 17 additionally comprising a collagenous material.

20. The stent of claim 20 where the tubular member comprises porous polytetrafluoroethylene and a collagenous material at least partially fills the pores of said porous polytetrafluoroethylene tubular member.

21. The stent of claim 4 where the tubular member comprises a polymeric non-thrombogenic material.

22. The stent of claim 17 where the tubular graft member is substantially coaxial with the passageway and interior to the cylinder and distributively and slidably connected to said stent component.

23. The stent of claim 22 wherein the tubular graft member is connected to the flexible link.

24. A method for the introduction of stent into a body lumen comprising the steps of:

introducing a collapsed stent having two ends and a longitudinal axis between those ends and comprising at least one assembly comprising at least one torsion member, said torsion member being situated so that when said assembly is distorted, said torsion member is twisted, to a selected site in a body lumen,

releasing the collapsed stent so to cause a twisted torsion member to untwist and to expand the stent at the selected site in a body lumen.

25. The method of claim 24 wherein said stent does not change in length during collapsing or releasing of the stent.

26. The method of claim 24 in which the selected site is vascular.

27. The method of claim 24 in which the stent is folded.

28. The method of claim 27 in which the folded stent is held in a collapsed condition prior to release by a sliding sheath exterior to the collapsed stent.

29. The method of claim 27 in which the folded stent is held in a collapsed condition prior to release by a slip line interwoven with said stent.

30. The method of claim 29 in which the slip line is in the form of a sack knot.

31. The method of claim 24 in which the stent is metallic.

32. The method of claim 31 in which the stent is a super-elastic alloy.

33. The method of claim 31 in which the stent is nitinol.

34. The method of claim 24 where the stent, after release, comprises a generally cylindrical form with two ends, a passageway having a radius extending between those ends, and an axis extending along said passageway, where said stent comprises

at least one helically aligned torsion member defining said cylinder, and said helically aligned torsion member has undulating elements, and

at least one flexible link passing through said undulating elements on adjacent helical turns.

35. The method of claim 34 where said undulating elements are arranged in an intercooperating phased relationship between adjacent helical turns.

36. The method of claim 35 where said flexible link maintains said undulating elements in phased relationship between adjacent helical turns.

37. The method of claim 24 wherein the stent further comprises a tubular member coaxial to at least a portion of the passageway.

38. The method of claim 37 wherein the tubular member is frangible.

39. The method of claim 37 in which the tubular is a polymeric nonthrombogenic material.

40. The method of claim 37 where the tubular member comprises a material selected from polyethylene, polypropylene, polyglycolic acid, polyesters, polyamides, their mixtures, blends, copolymers, mixtures, blends and copolymers; polyesters, polyaramids, polyfluorocarbons, and porous or nonporous polyurethanes; and collagenous materials.

41. The method of claim 40 where the tubular member comprises porous or non-porous polytetrafluoroethylene.

42. The method of claim 40 additionally comprising a collagenous material.

43. The method of claim 42 where the tubular member comprises porous polytetrafluoroethylene and a collagenous material at least partially fills the pores of said porous polytetrafluoroethylene tubular member.

44. The method of claim 37 where the tubular member comprises a collagen-based material.

45. The method of claim 37 where the tubular member additionally comprises reinforcing fibers within said tubular member.

46. The method of claim 37 where the tubular member additionally comprises radiopaque fibers within said tubular member.

47. The method of claim 44 where the collagen-based material comprises a pharmaceutically acceptable collagen chemically conjugated to a synthetic hydrophilic polymer.

48. The method of claim 24 where the at least one assembly is at least one ring assembly extending circumferentially about said passageway, each said ring assembly containing at least one torsion member approximately parallel to said axis, said torsion member being situated so that when said ring assembly is distorted, said torsion member is twisted.

49. The method of claim 48 comprising more than one ring assembly.

50. The method of claim 49 where the ring assemblies are joined with tie members which are generally parallel to said axis.

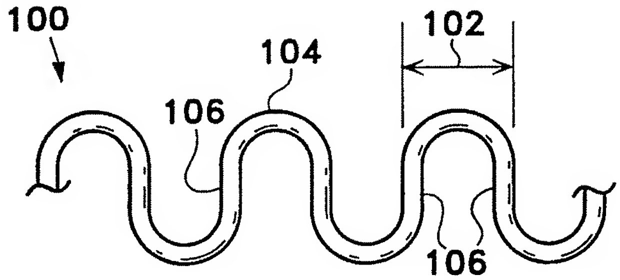


Fig. 1A

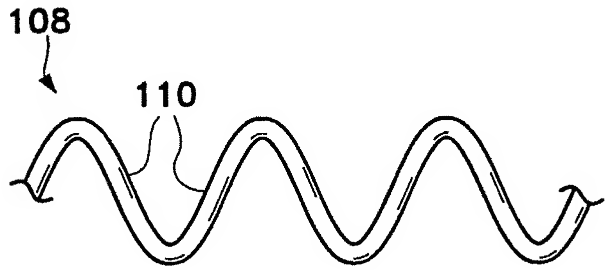


Fig. 1B

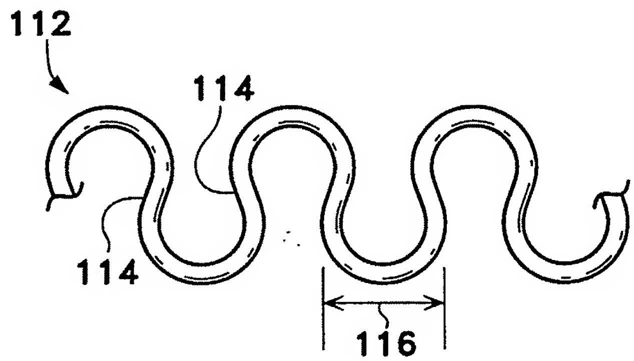


Fig. 1C

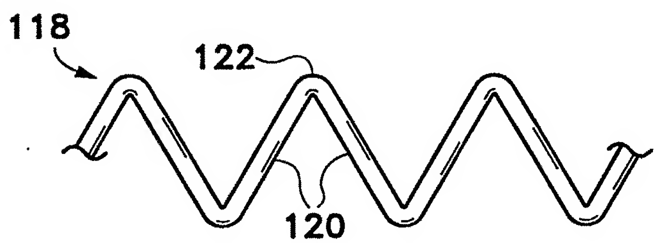


Fig. 1D

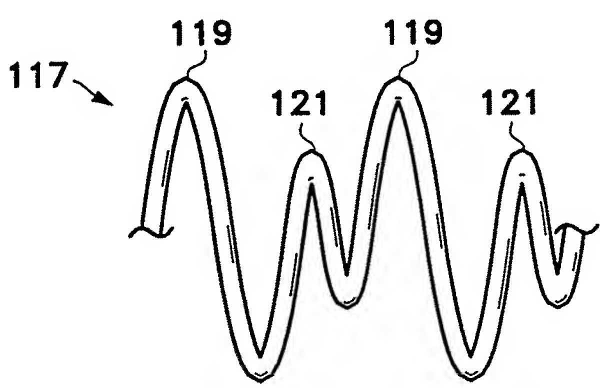


Fig. 1E

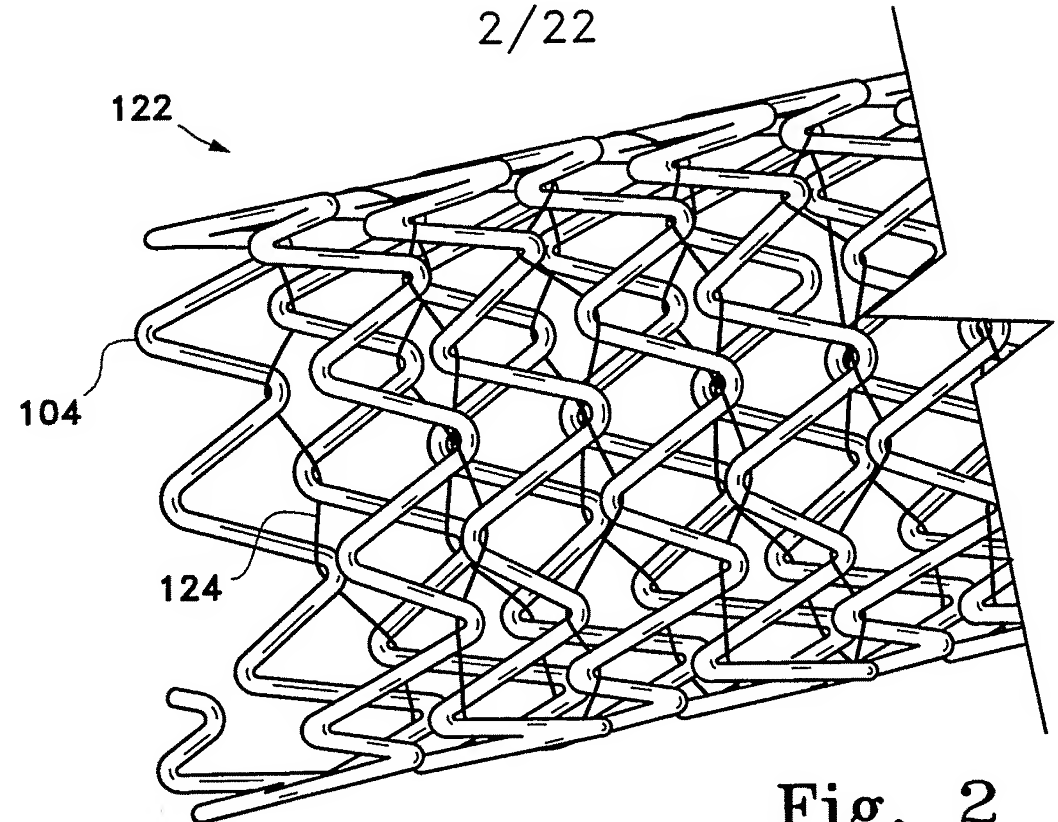


Fig. 2

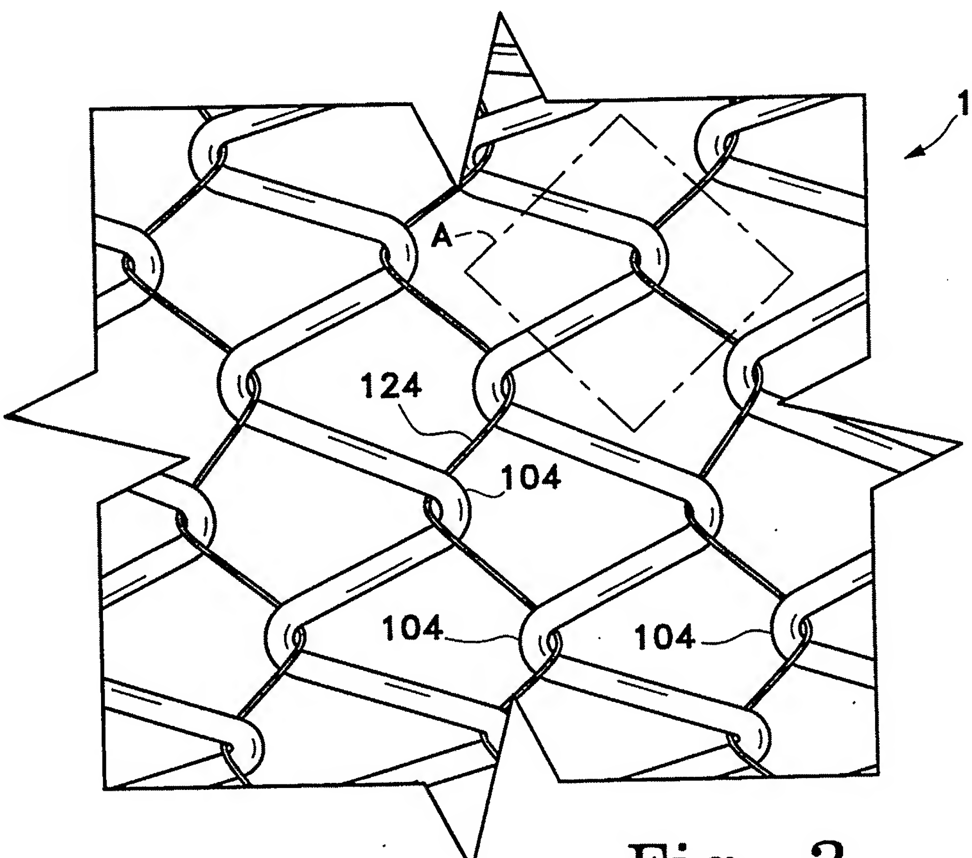


Fig. 3

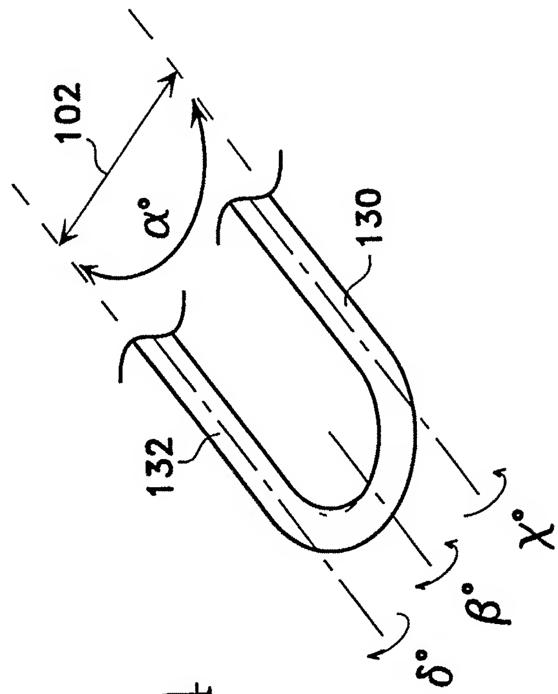


Fig. 4

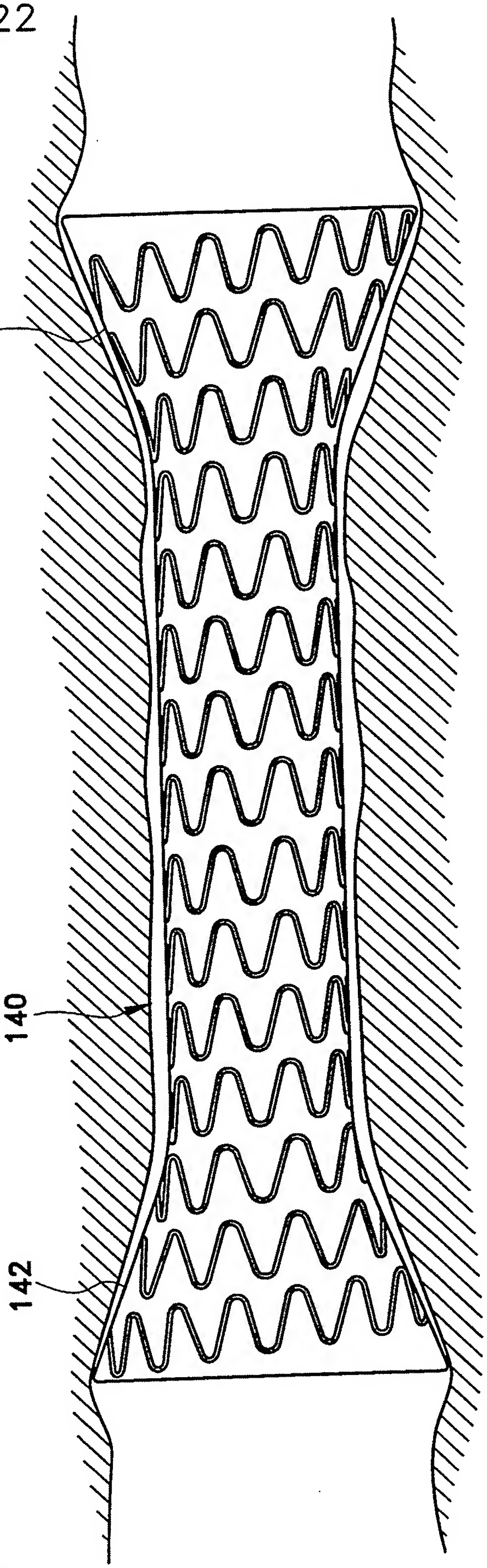


Fig. 5

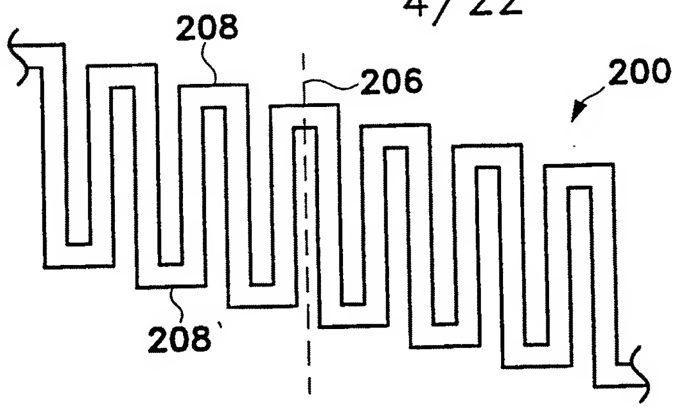


Fig. 6

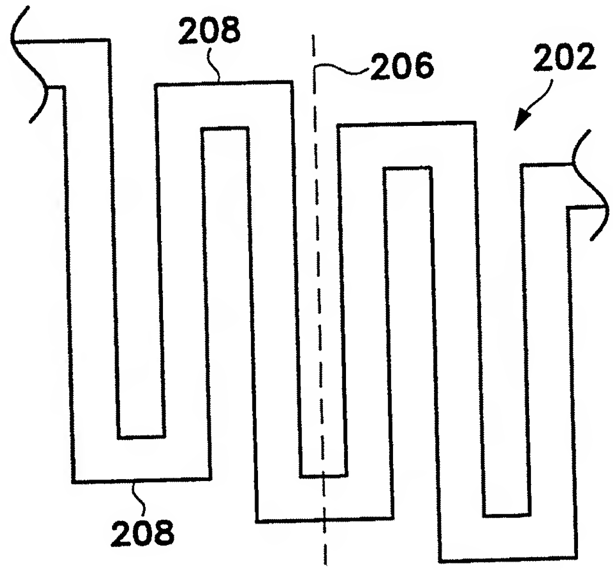


Fig. 7

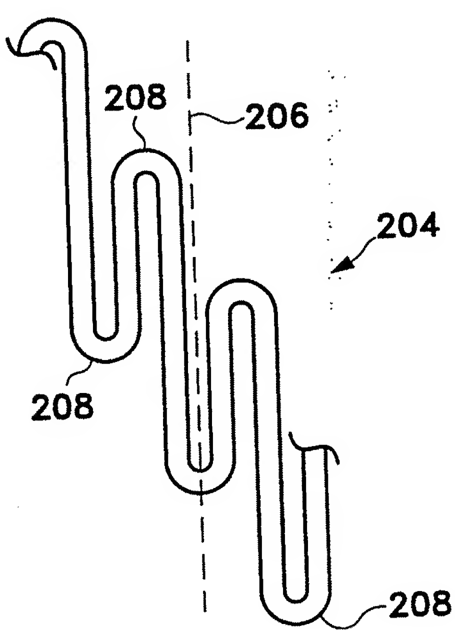
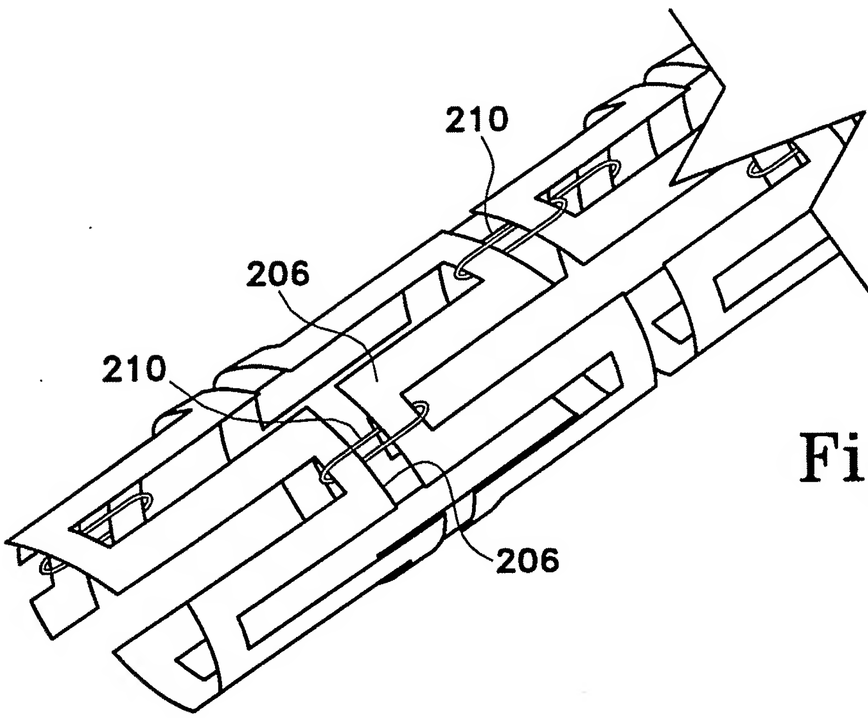


Fig. 8



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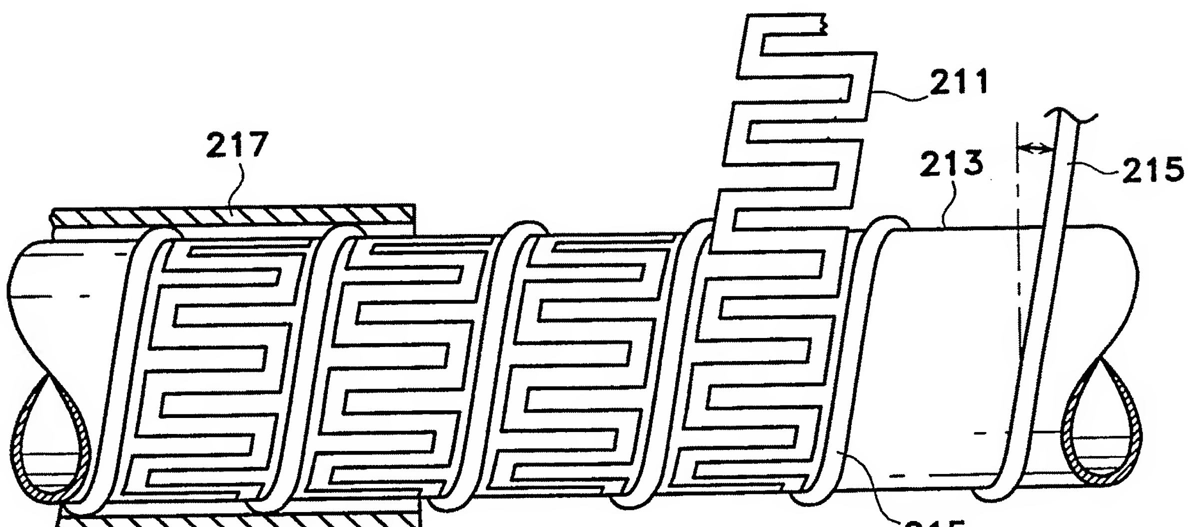

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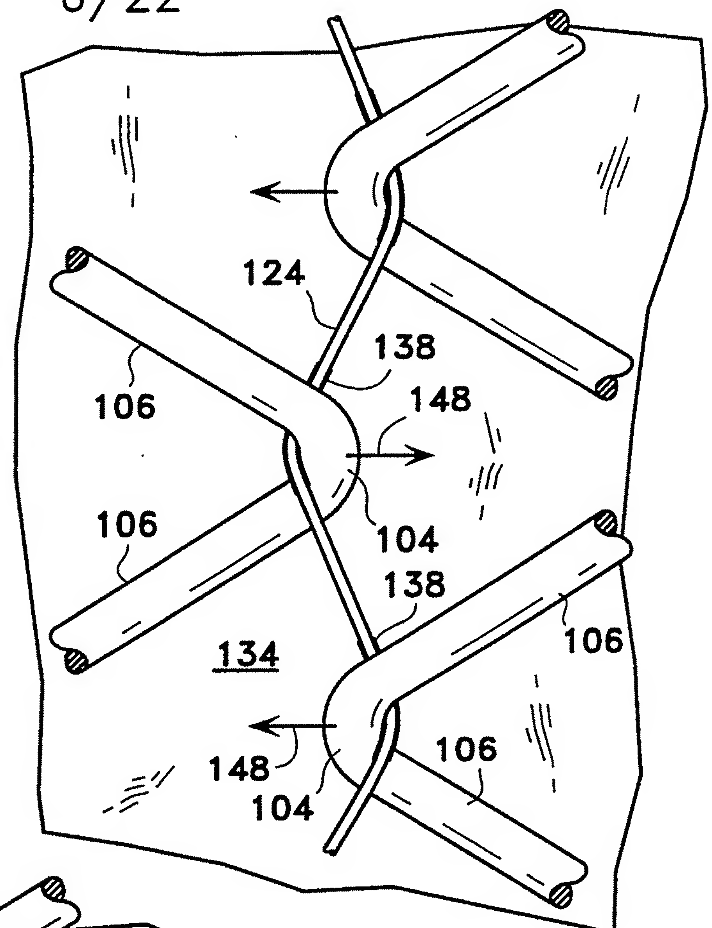
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Fig. 11

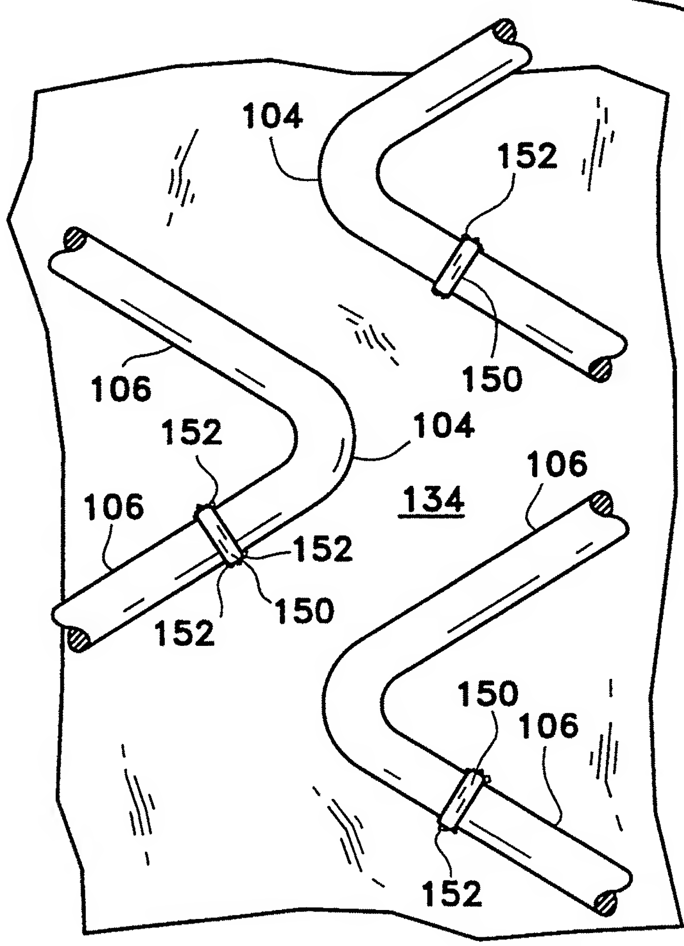
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Fig. 12

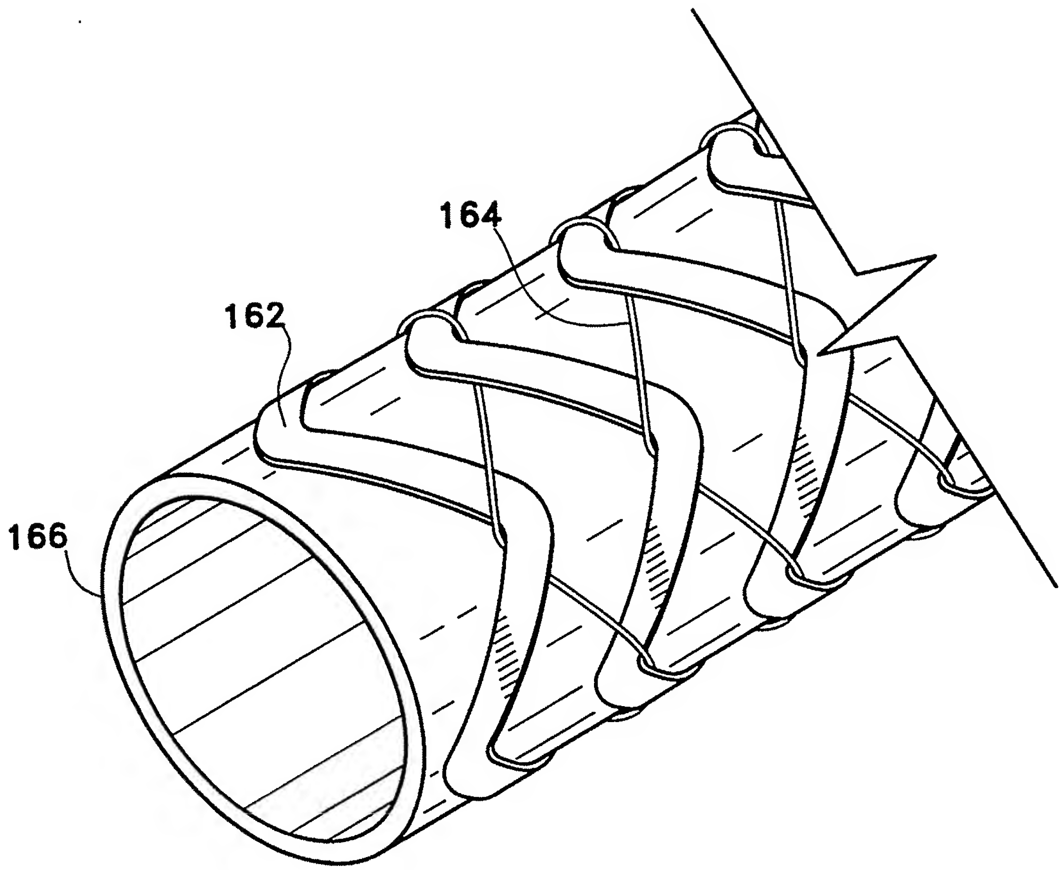

Fig. 13

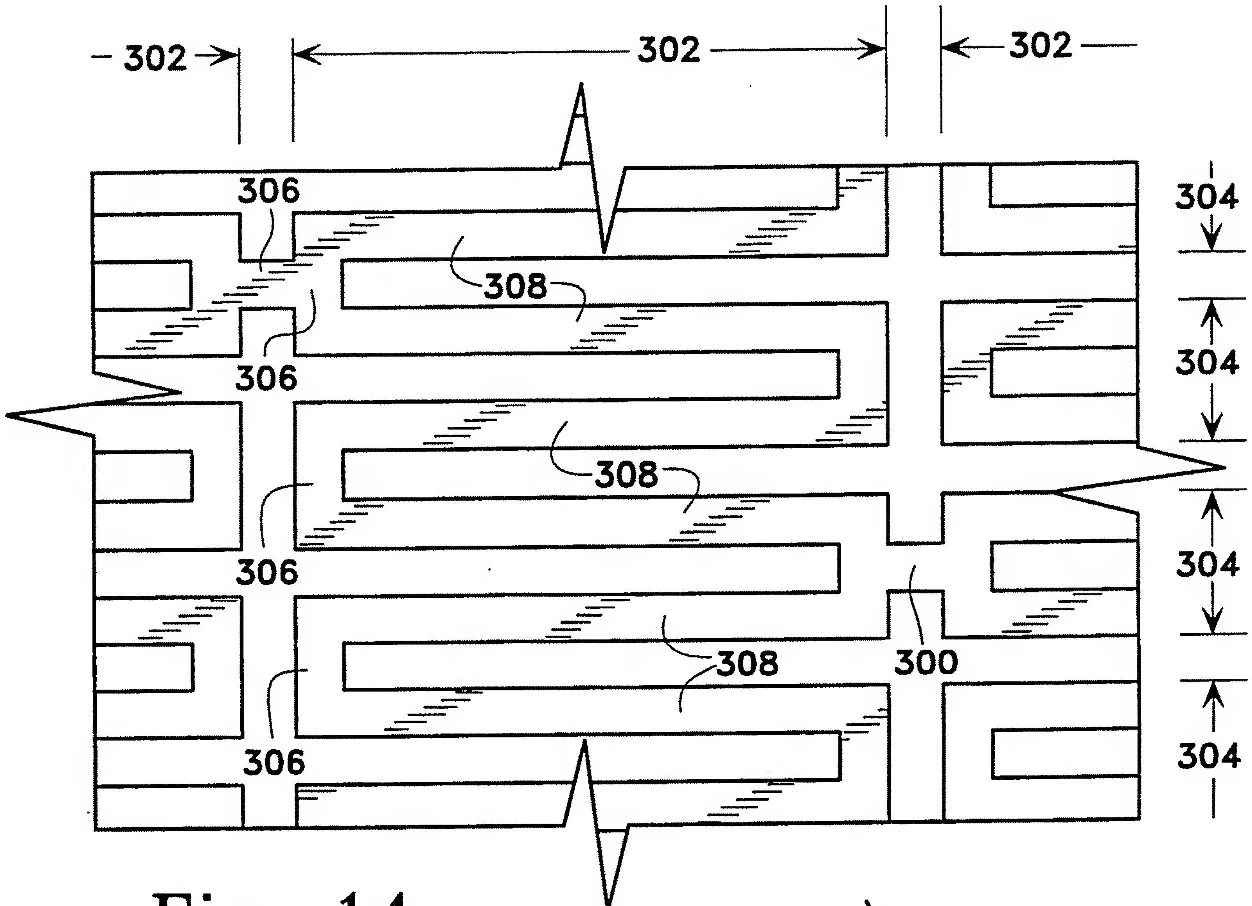

Fig. 14

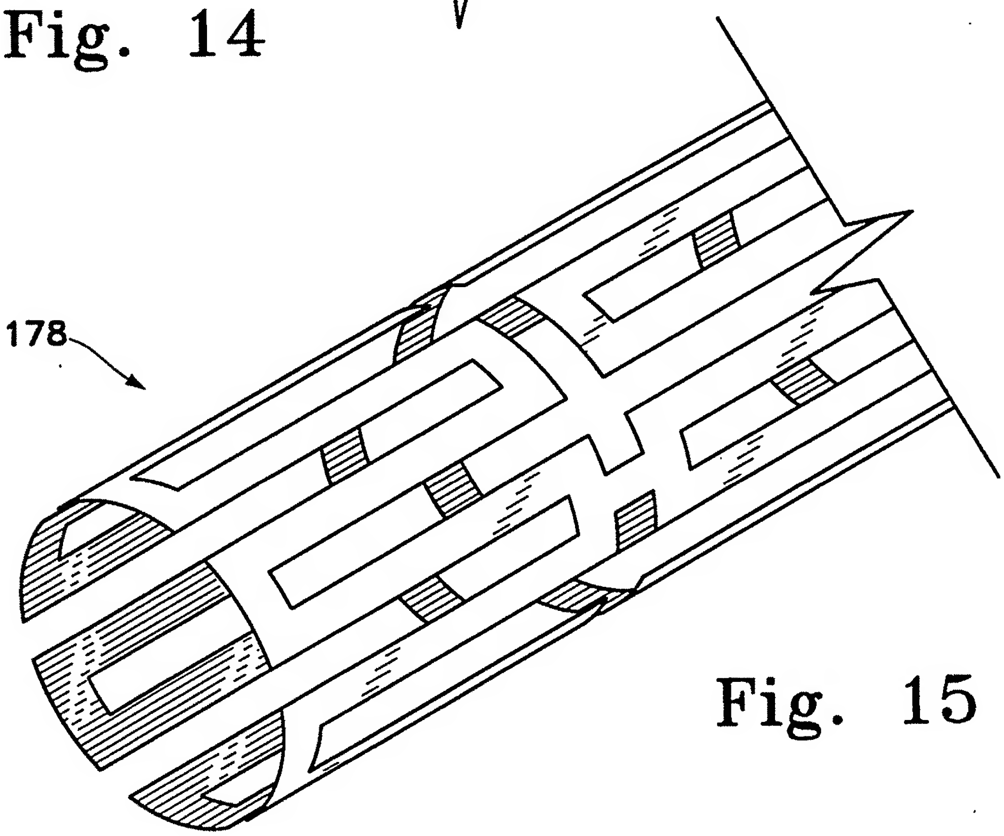

Fig. 15

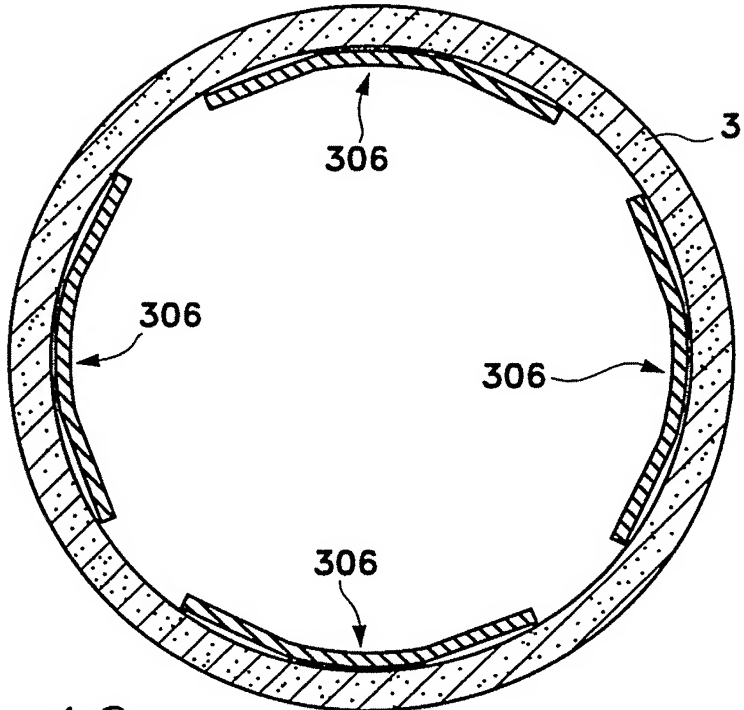

Fig. 16

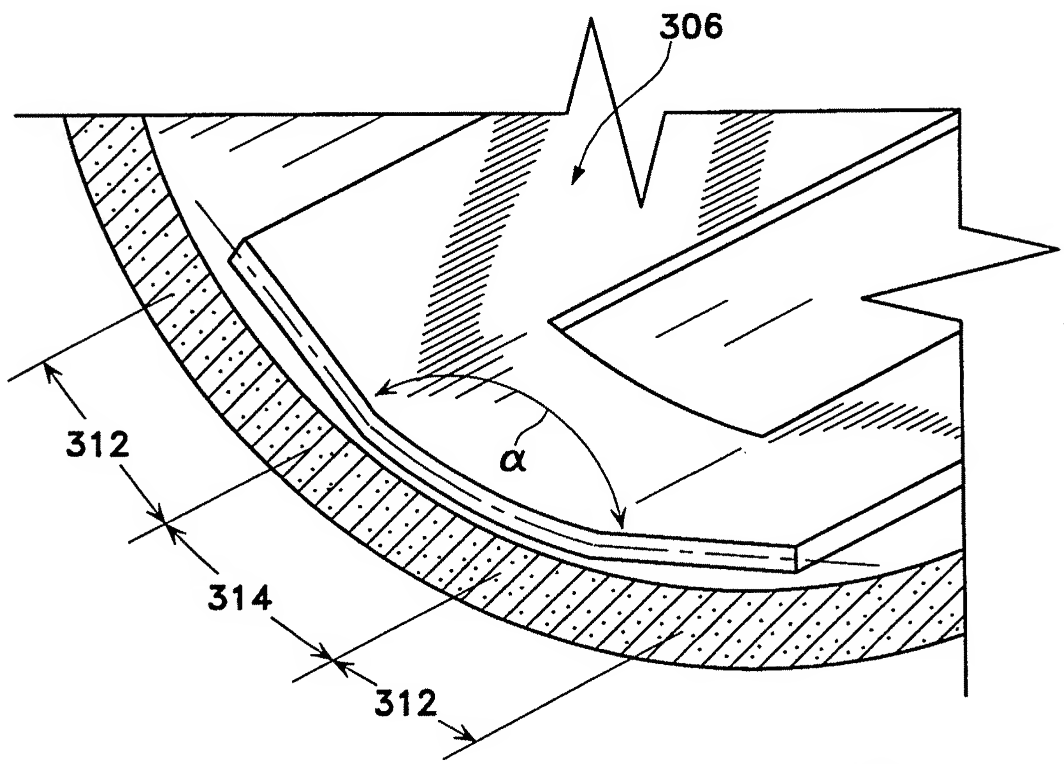

Fig. 17

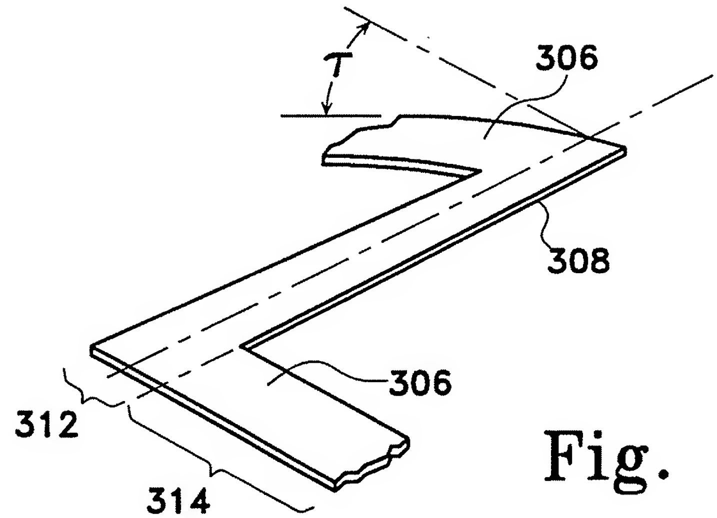

Fig. 18

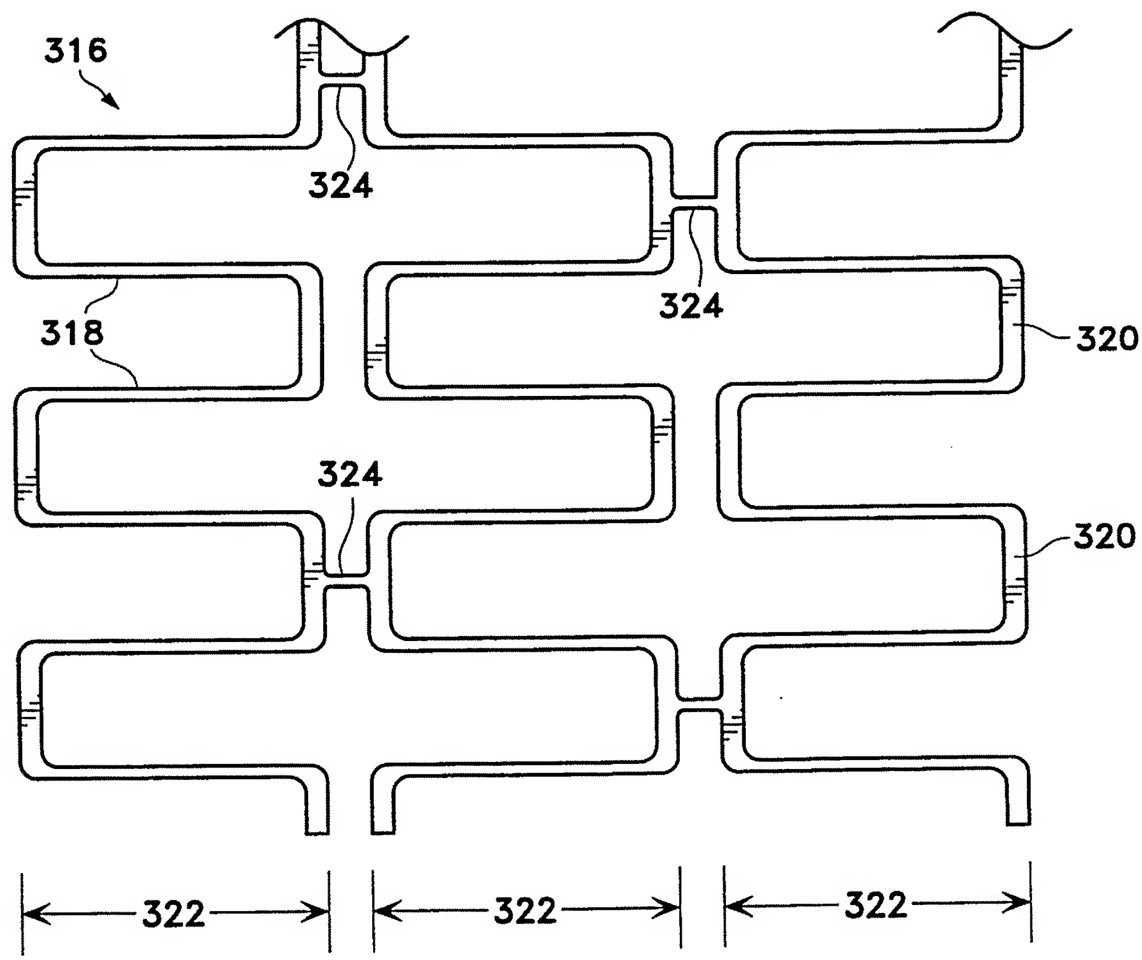

Fig. 19

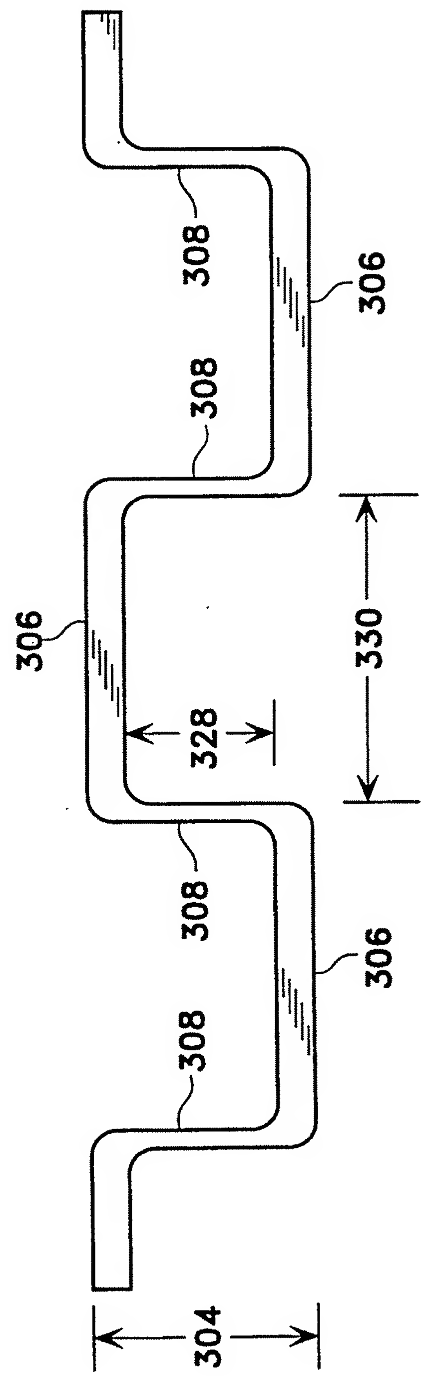

Fig. 20

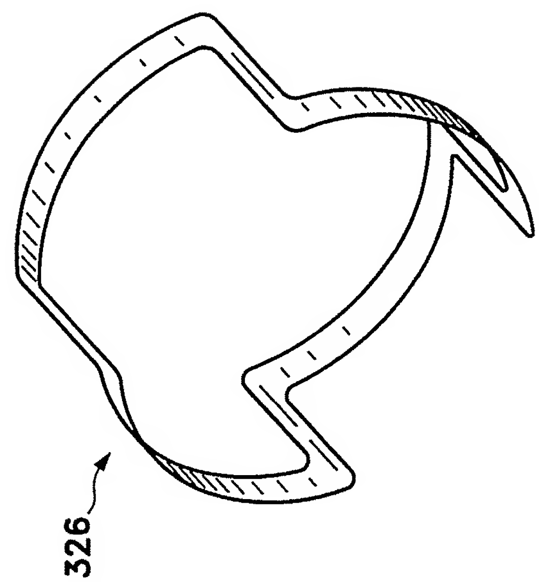

Fig. 21

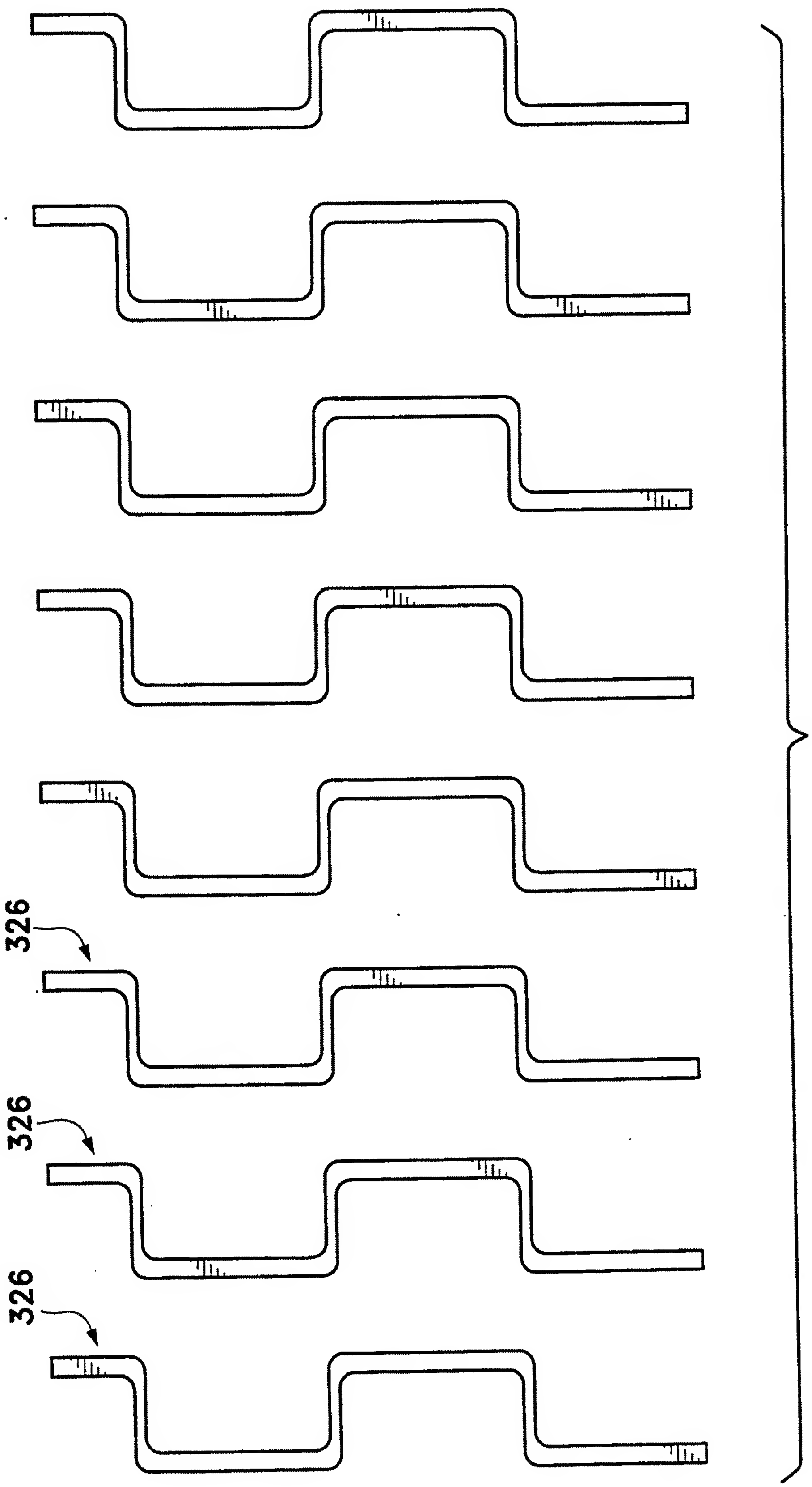

Fig. 22

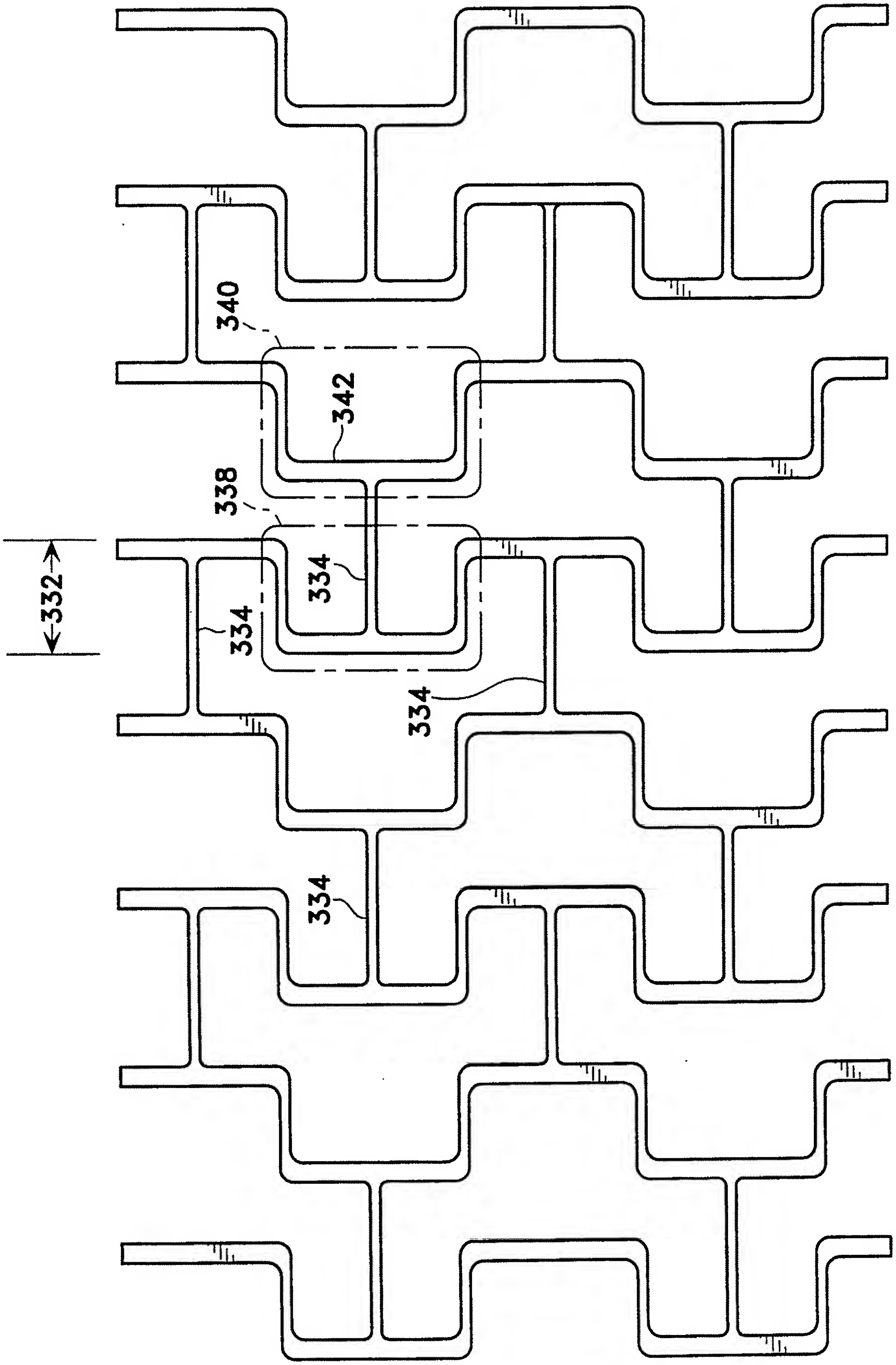

Fig. 23

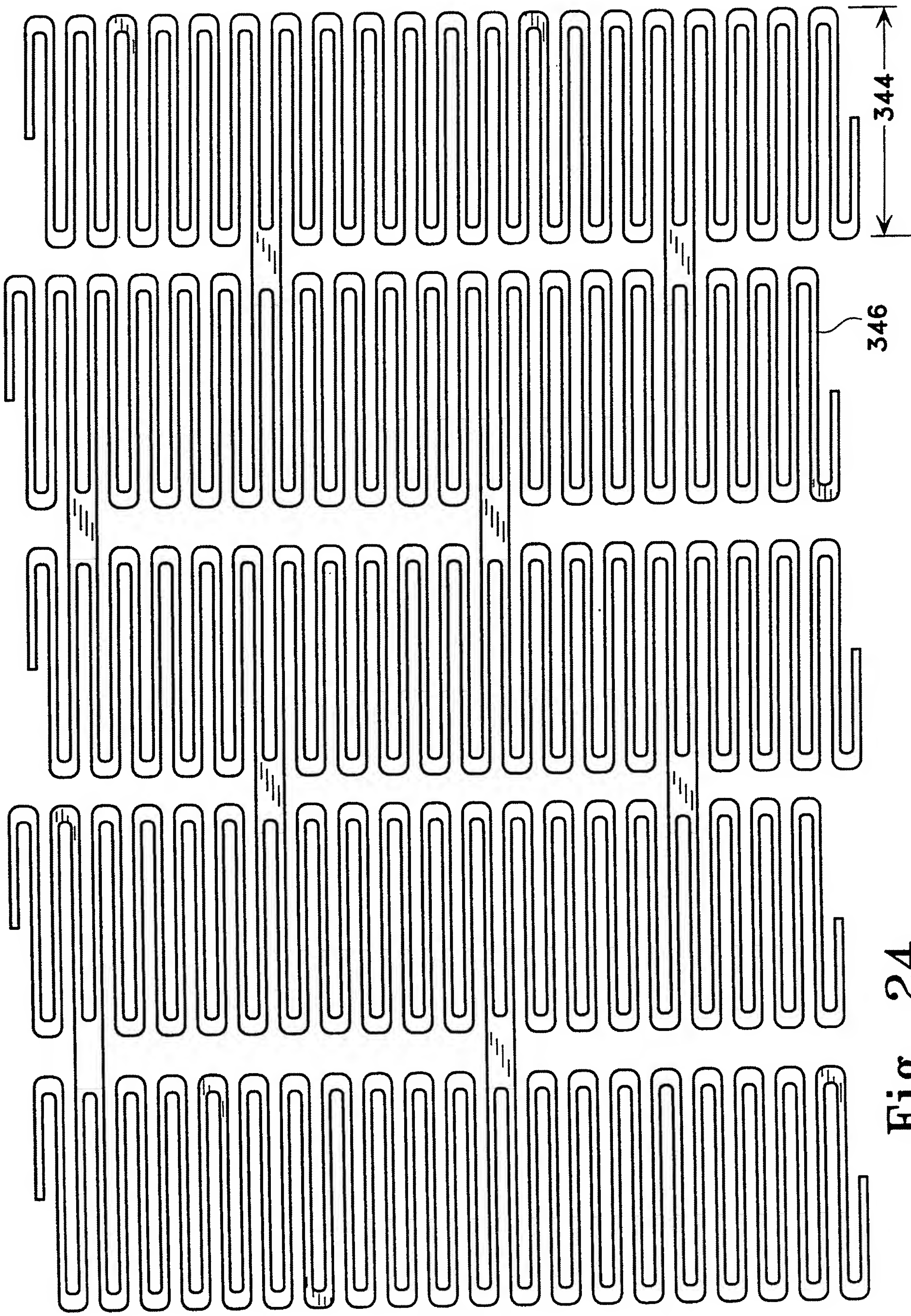

Fig. 24

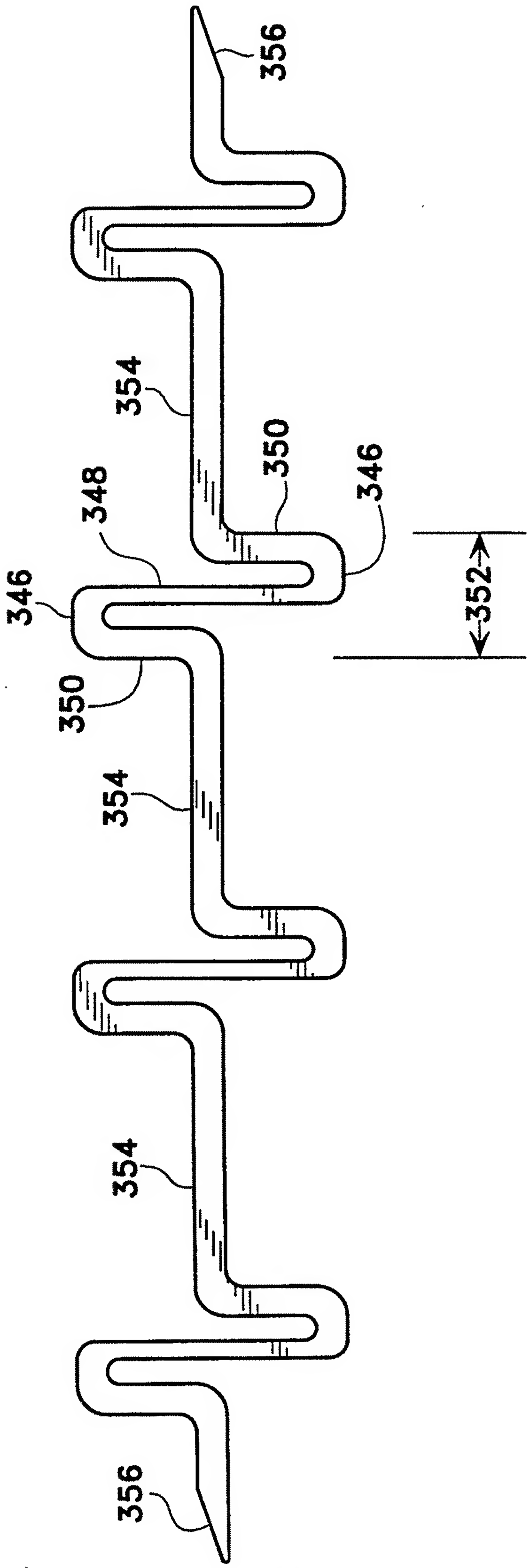

Fig. 25

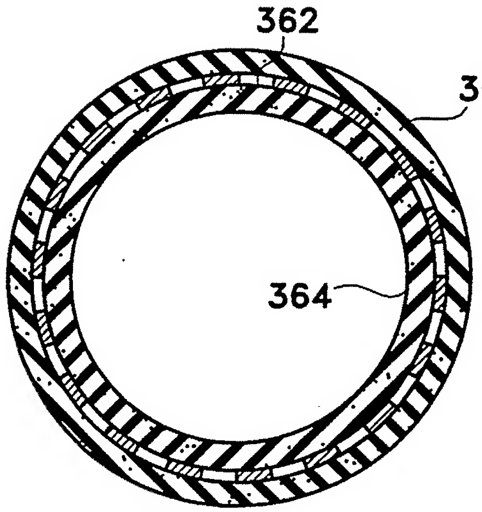

Fig. 26

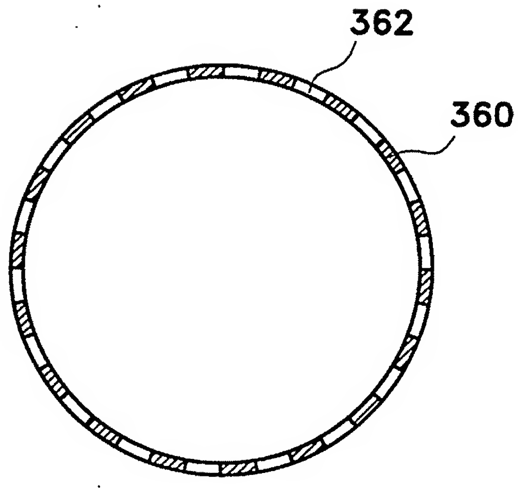

Fig. 27

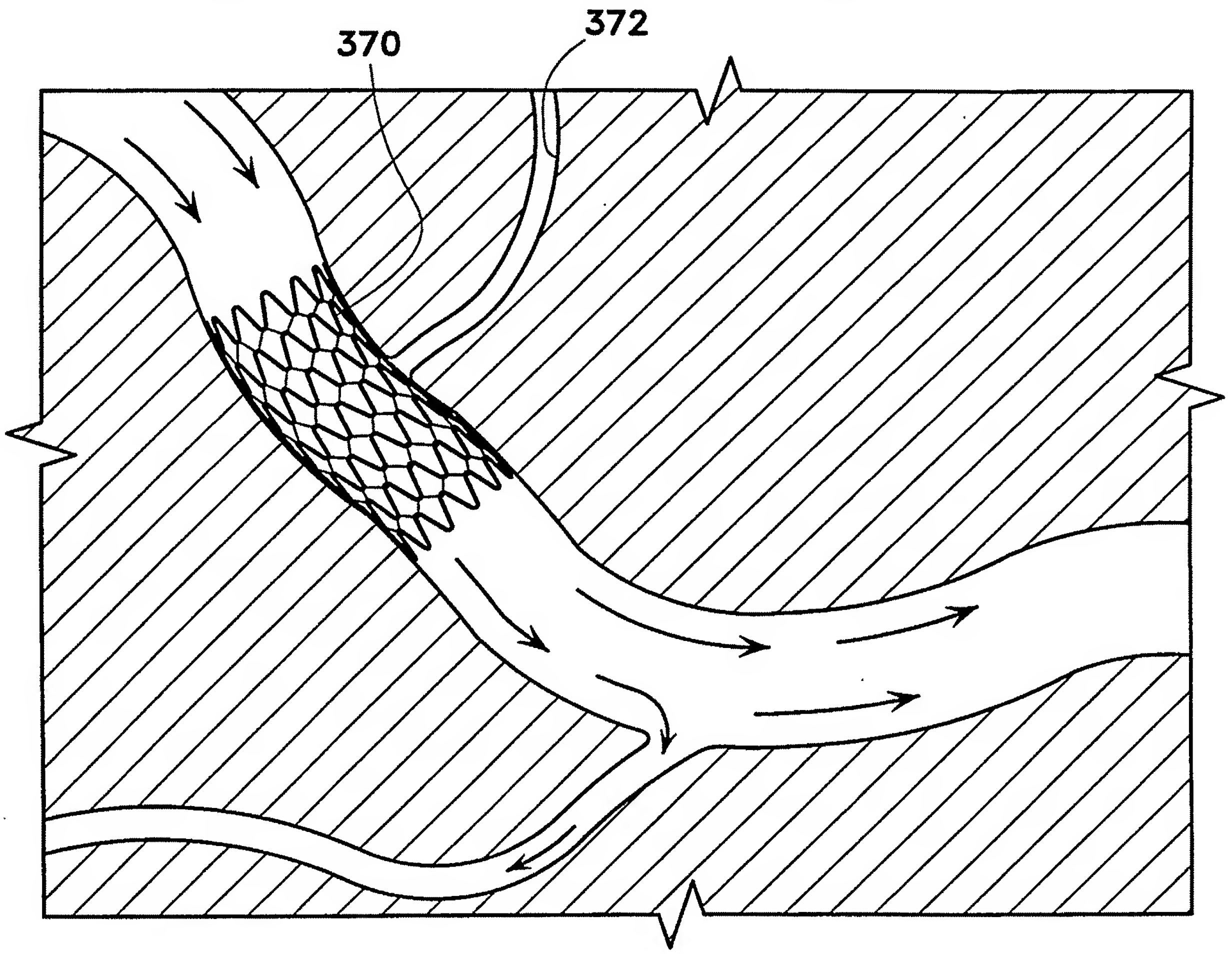

Fig. 28

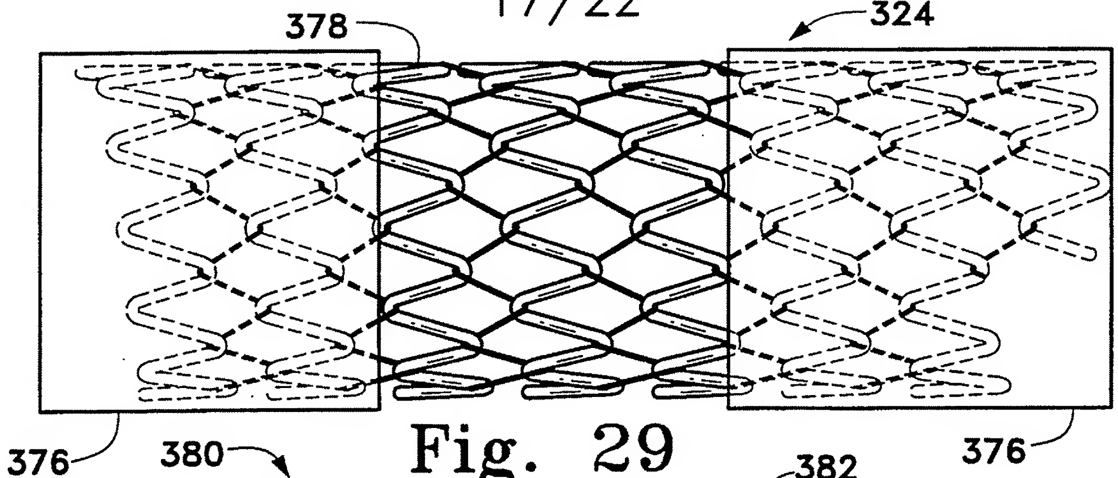

Fig. 29

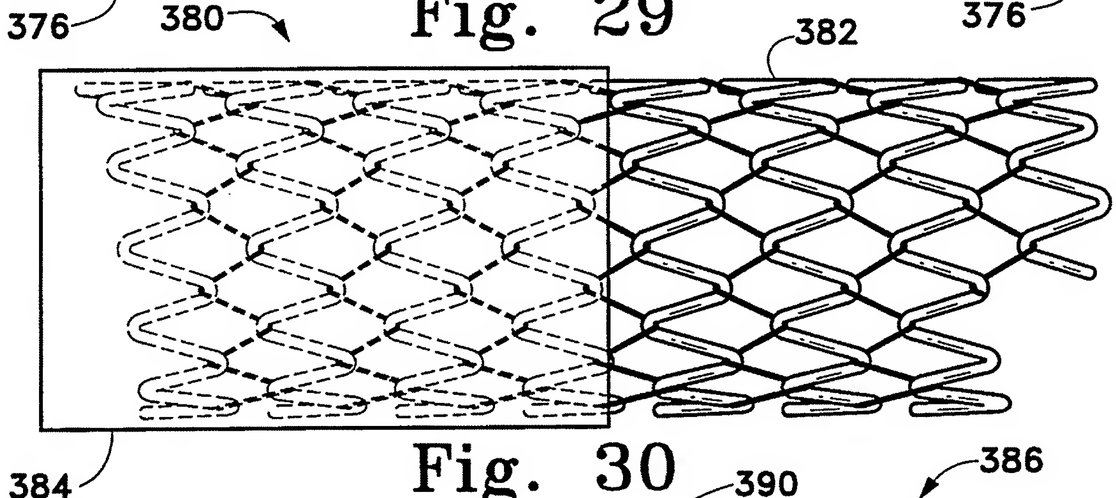

Fig. 30

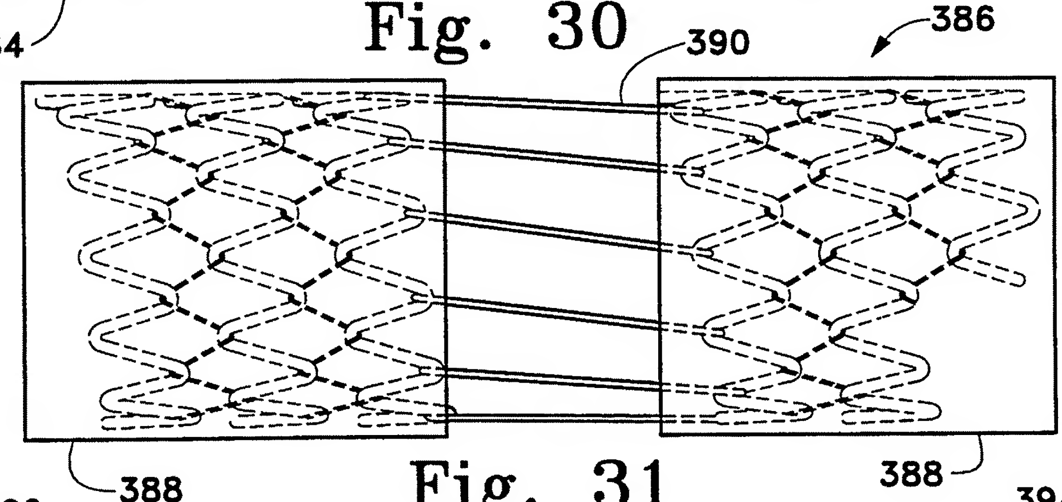

Fig. 31

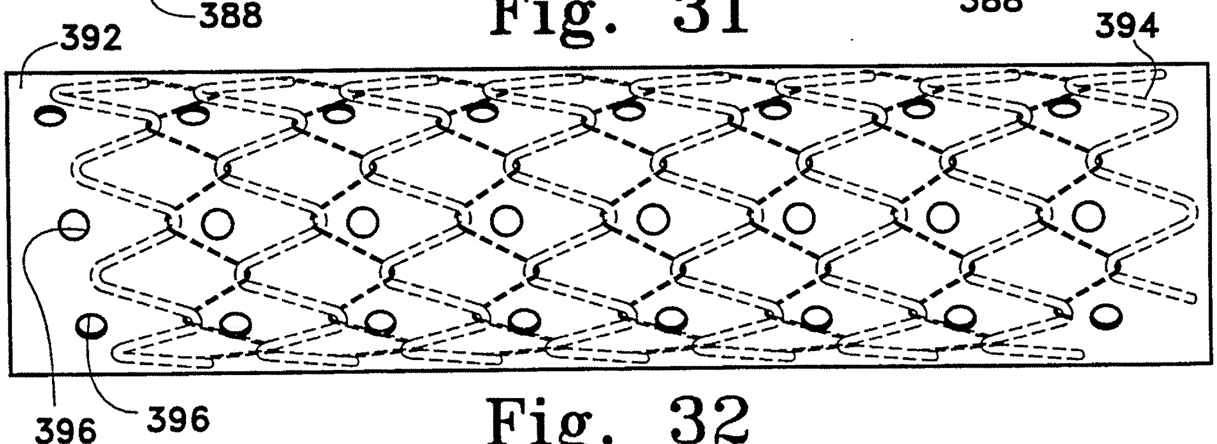

Fig. 32

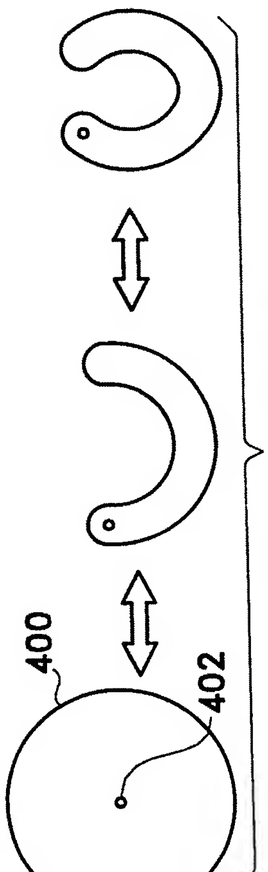

Fig. 33A

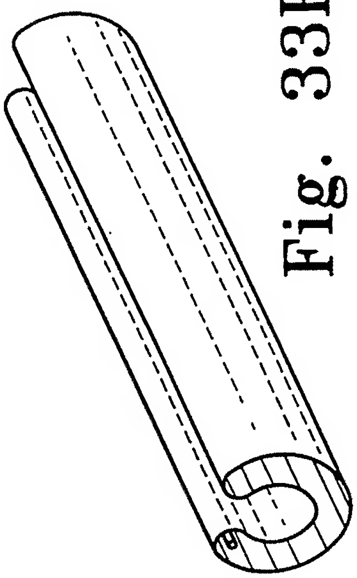

Fig. 33B

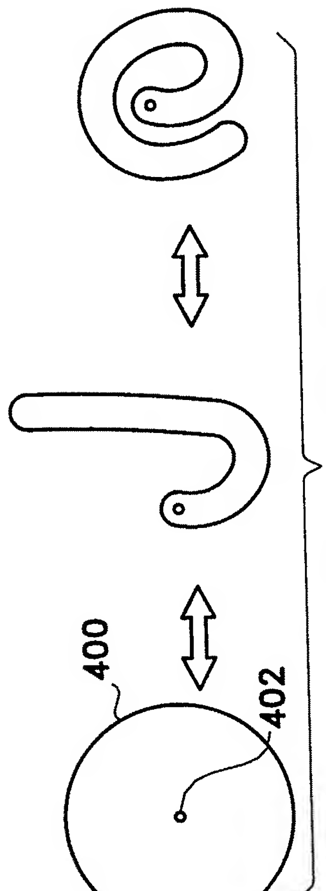

Fig. 33C

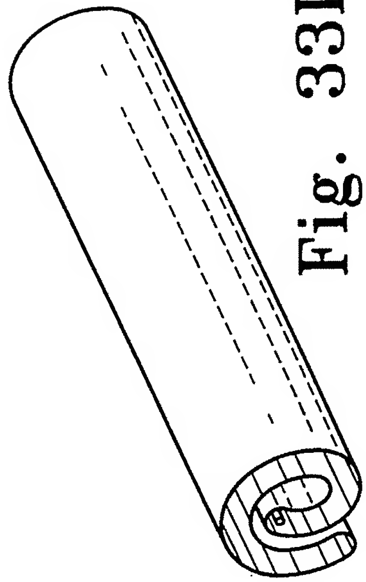

Fig. 33D

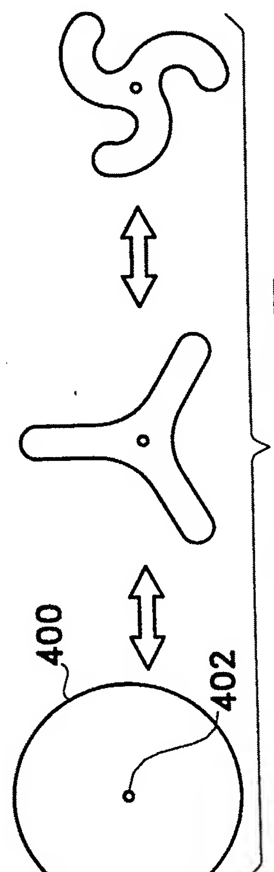

Fig. 33E

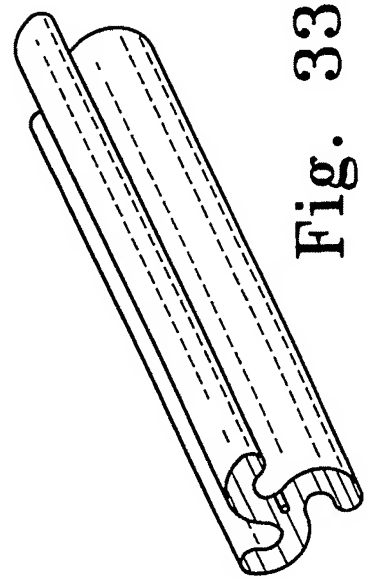

Fig. 33F

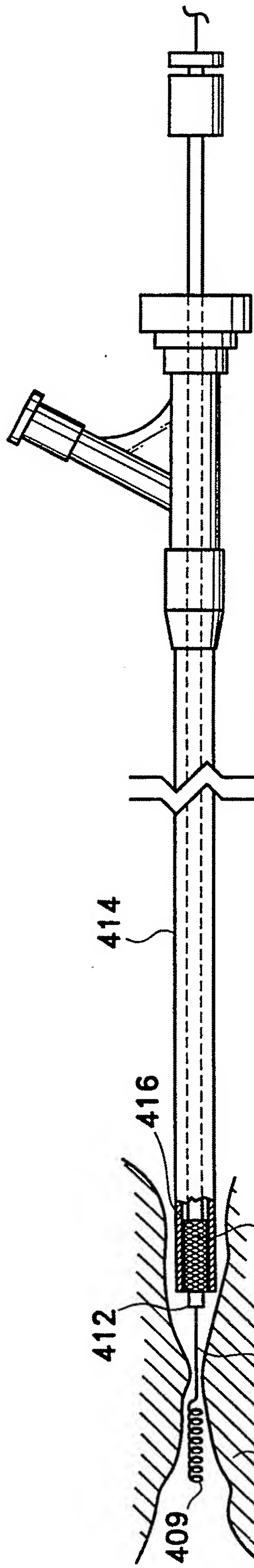

Fig. 34A

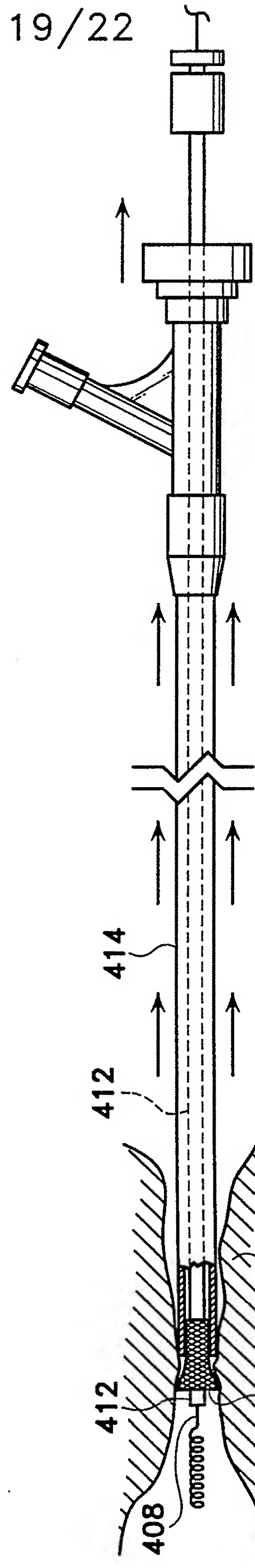

Fig. 34B

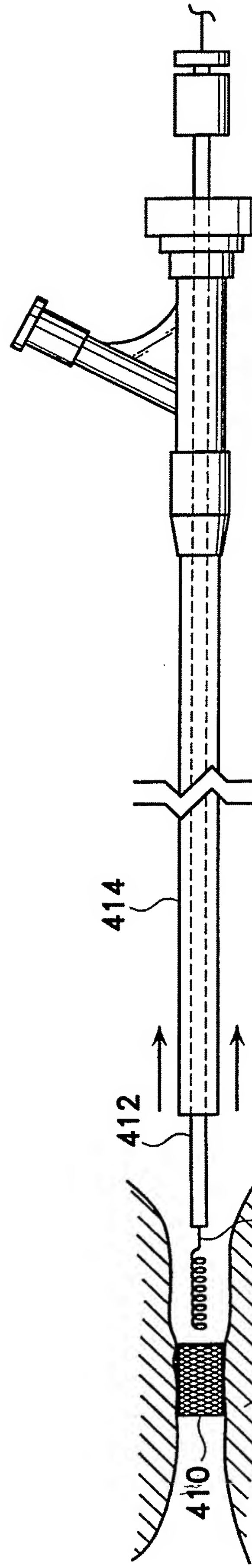

Fig. 34C

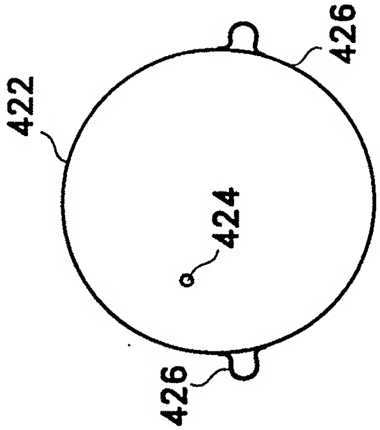

Fig. 35C

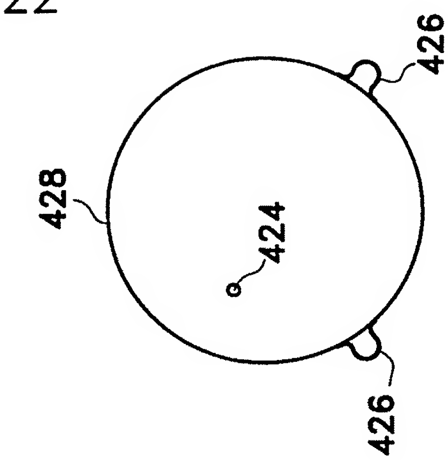

Fig. 36C

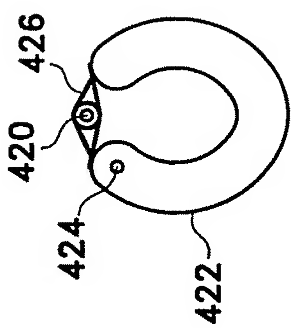

Fig. 35B

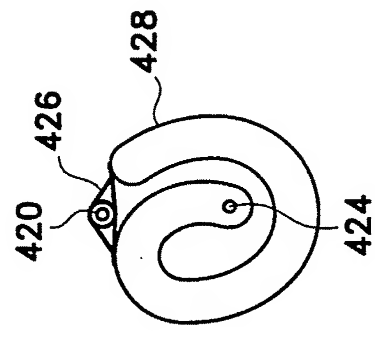

Fig. 36B

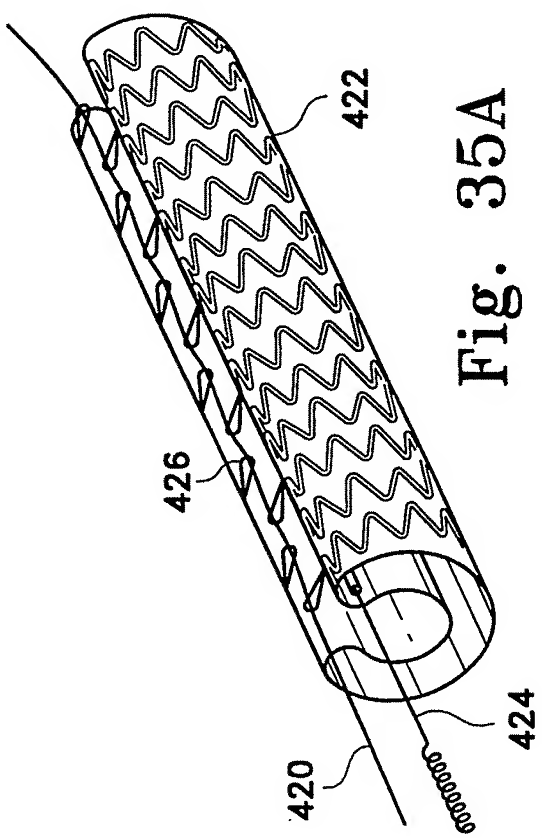

Fig. 35A

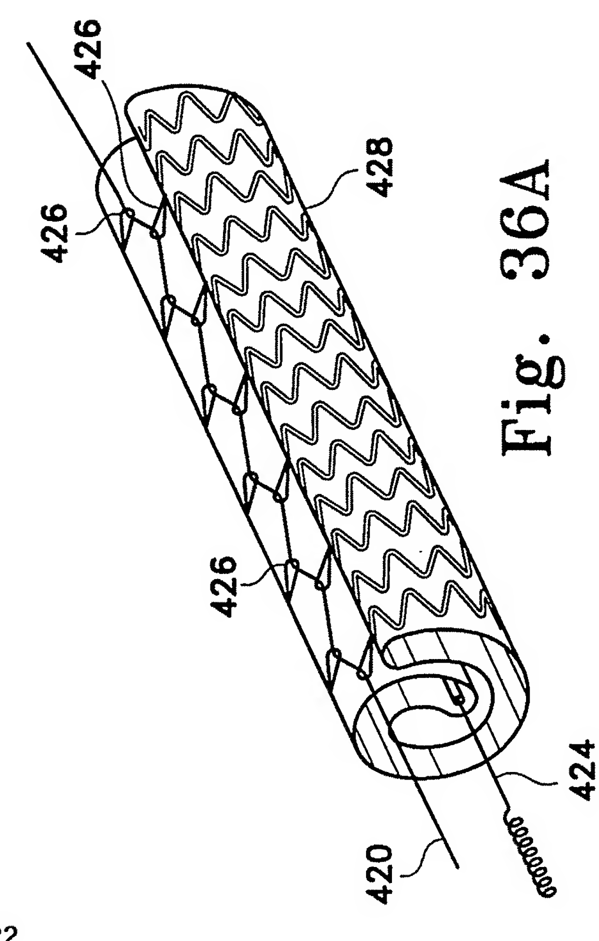

Fig. 36A

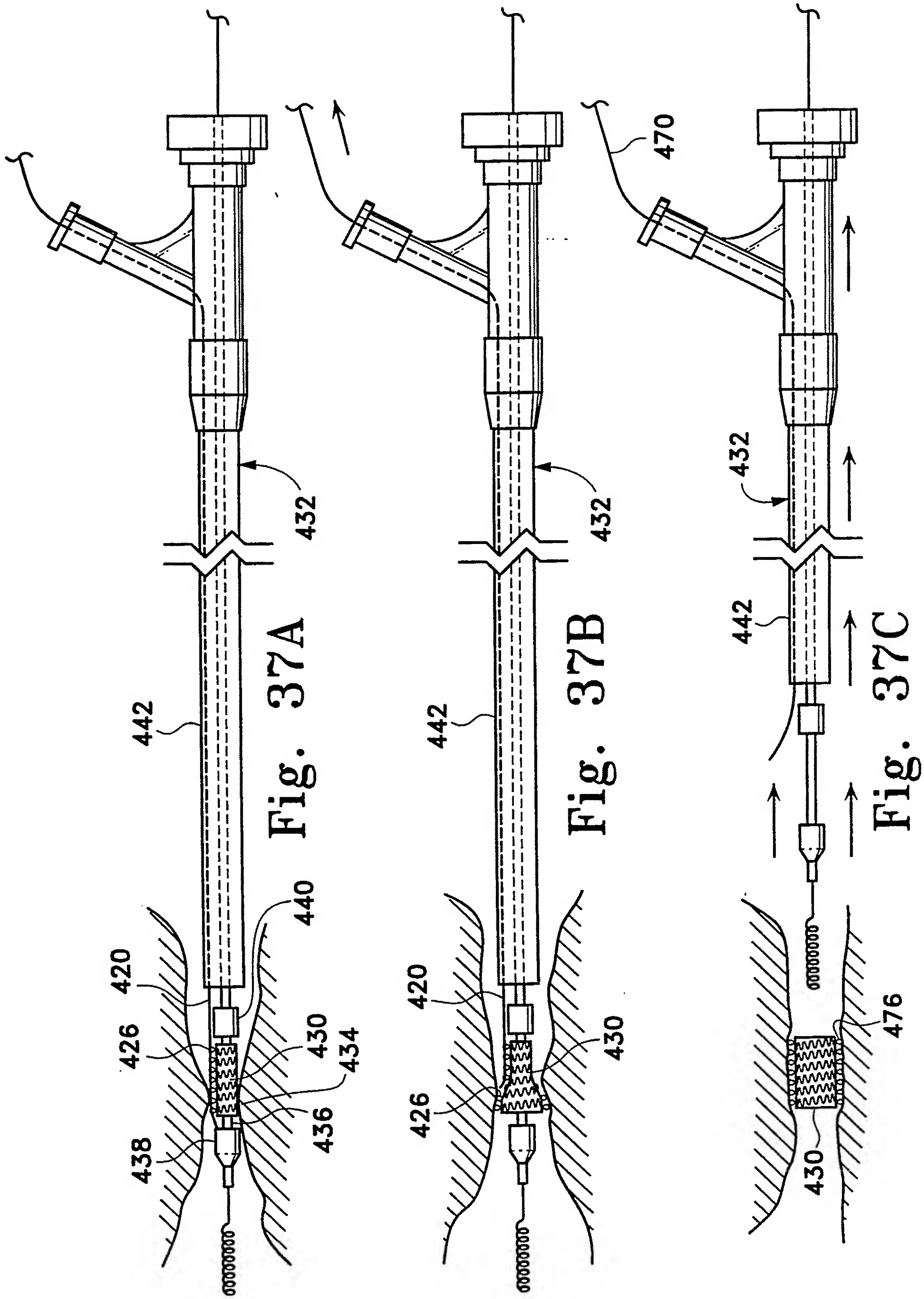

Fig. 37A

Fig. 37B

Fig. 37C

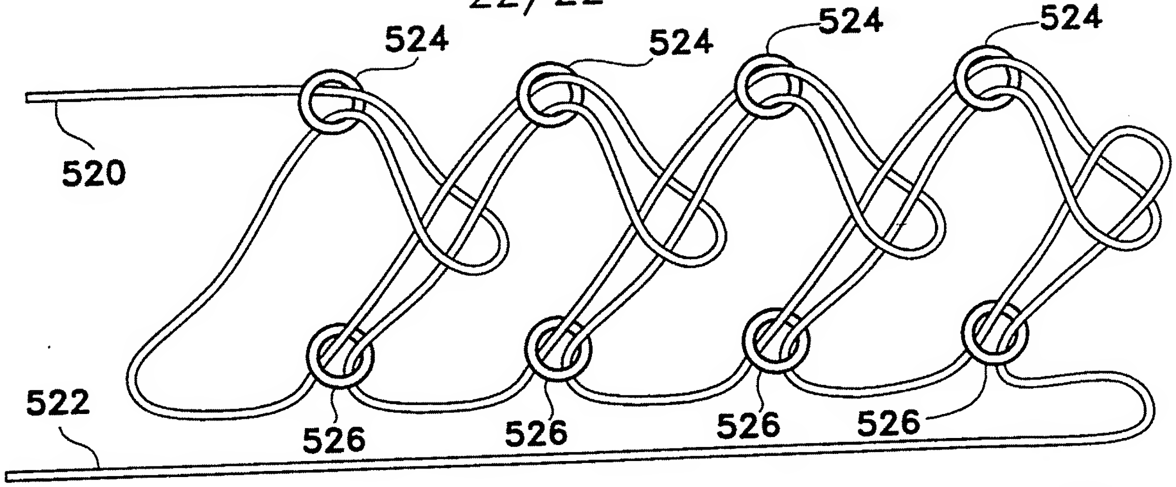

Fig. 38

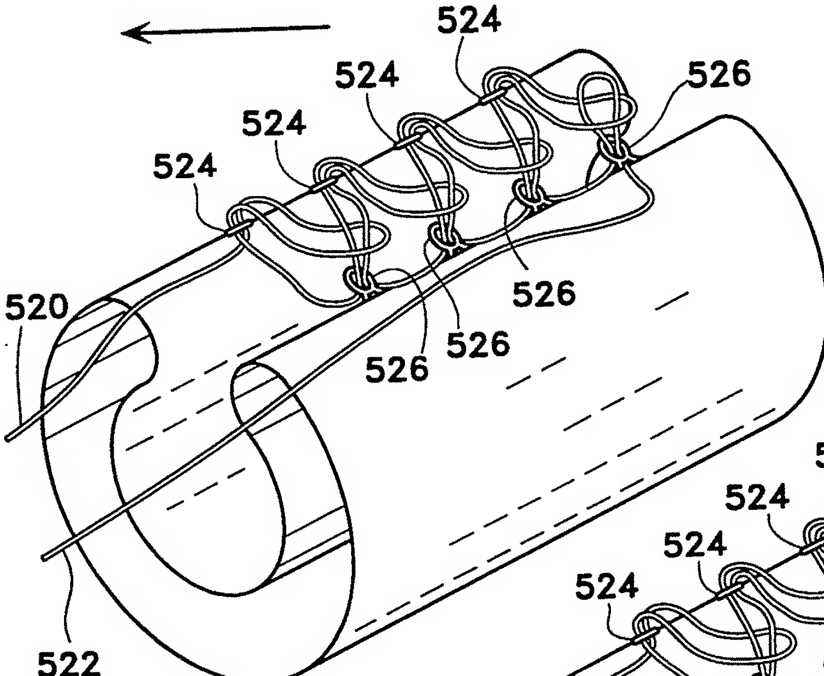

Fig. 39

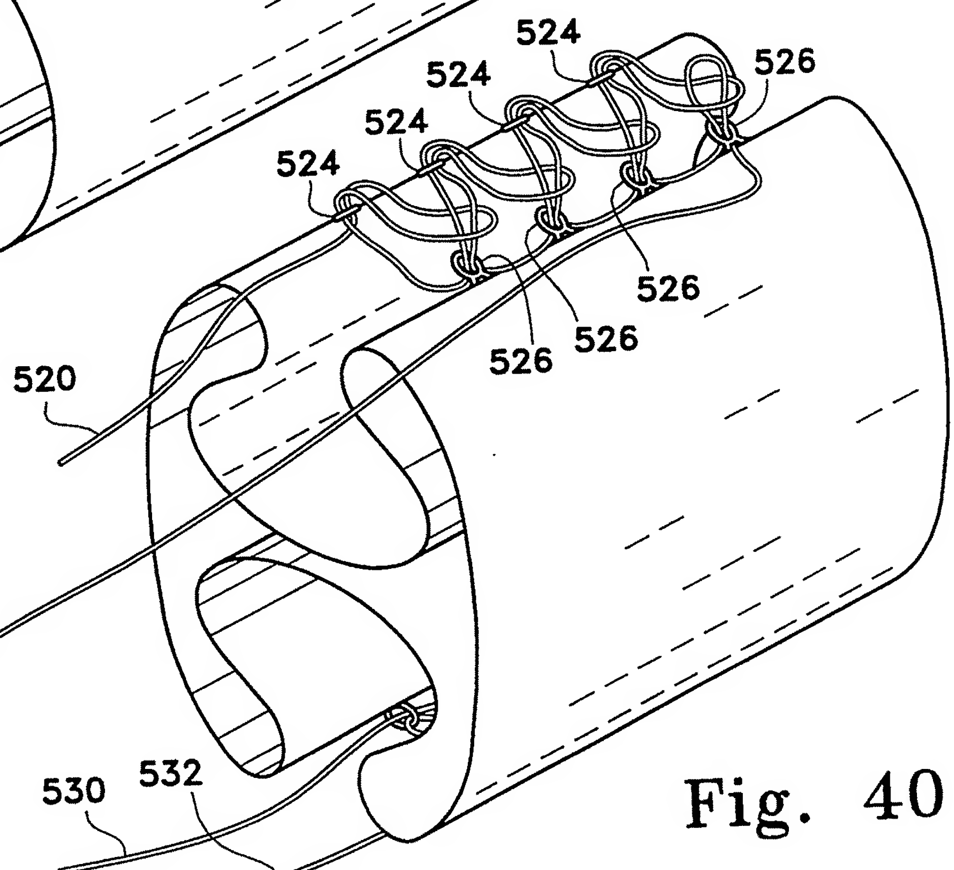

Fig. 40